

Organic Reactions

Organic Reactions

VOLUME 10

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PREFACE TO THE SERIES

In the course of nearly every program of research in organic chemistry the investigator finds it necessary to use several of the better-known synthetic reactions. To discover the optimum conditions for the application of even the most familiar one to a compound not previously subjected to the reaction often requires an extensive search of the literature; even then a series of experiments may be necessary. When the results of the investigation are published, the synthesis, which may have required months of work, is usually described without comment. The background of knowledge and experience gained in the literature search and experimentation is thus lost to those who subsequently have occasion to apply the general method. The student of preparative organic chemistry faces similar difficulties. The textbooks and laboratory manuals furnish numerous examples of the application of various syntheses, but only rarely do they convey an accurate conception of the scope and usefulness of the processes.

For many years American organic chemists have discussed these problems. The plan of compiling critical discussions of the more important reactions thus was evolved. The volumes of *Organic Reactions* are collections of chapters each devoted to a single reaction, or a definite phase of a reaction, of wide applicability. The authors have had experience with the processes surveyed. The subjects are presented from the preparative viewpoint, and particular attention is given to limitations, interfering influences, effects of structure, and the selection of experimental techniques. Each chapter includes several detailed procedures illustrating the significant modifications of the method. Most of these procedures have been found satisfactory by the author or one of the editors, but unlike those in *Organic Syntheses* they have not been subjected to careful testing in two or more laboratories. When all known examples of the reaction are not mentioned in the text, tables are given to list compounds which have been prepared by or subjected to the reaction. Every effort has been made to include in the tables all such compounds and references; however, because of the very nature of the reactions discussed and their frequent use as one of the several steps of syntheses in which not all of the intermediates have been isolated, some instances may well have been missed. Nevertheless, the investigator will be able

to use the tables and their accompanying bibliographies in place of most or all of the literature search so often required.

Because of the systematic arrangement of the material in the chapters and the entries in the tables, users of the books will be able to find information desired by reference to the table of contents of the appropriate chapter. In the interest of economy the entries in the indices have been kept to a minimum, and, in particular, the compounds listed in the tables are not repeated in the indices.

The success of this publication, which will appear periodically, depends upon the cooperation of organic chemists and their willingness to devote time and effort to the preparation of the chapters. They have manifested their interest already by the almost unanimous acceptance of invitations to contribute to the work. The editors will welcome their continued interest and their suggestions for improvements in *Organic Reactions*.

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CHAPTER 1

THE COUPLING OF DIAZONIUM SALTS WITH ALIPHATIC CARBON ATOMS

STANLEY M. PARMEYTER
Wheaton College

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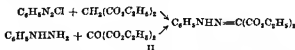
INTRODUCTION

A diazonium salt will couple with an aliphatic compound containing an activated carbon-hydrogen bond. This discussion is limited to those reactions in which both nitrogen atoms of the diazonium salt are retained in the resulting molecule. The discussion is further limited by the exclusion of coupling reactions which occur with the elimination of a group from an activated methinyl compound, the Japp-Klingemann reaction, as these reactions are discussed in Chapter 2.

Victor Meyer was the first to report the coupling of a diazonium salt with an activated aliphatic carbon atom.¹ He found that benzenediazonium sulfate reacts with the sodium salt of nitroethane to give a colored product which was assigned the azo structure I.



Coupling with other nitroparaffins²⁻⁵ as well as with ethylacetoacetate^{6,7} was soon reported. A question regarding the structure of the reaction products arose when it was discovered that benzenediazonium chloride coupled with diethyl malonate to give a product identical with the phenylhydrazone of diethyl mesoxalate (II)^{8a}



Much of the early work with the coupling reaction was prompted by the desire to determine whether the products were of the azo or hydrazone

¹ Meyer and Ambühl, *Ber.*, 8, 761 (1875).

² Meyer and Ambühl, *Ber.*, 8, 1073 (1875).

³ Fries, *Ber.*, 8, 1078 (1875).

⁴ Meyer, *Ber.*, 9, 384 (1876).

⁵ Zublin, *Ber.*, 10, 2087 (1877).

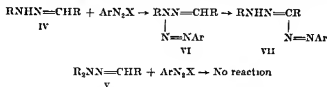
⁶ Meyer, *Ber.*, 10, 2075 (1877).

⁷ Zublin, *Ber.*, 11, 1417 (1878).

^{8a} Meyer, *Ber.*, 21, 118 (1888).

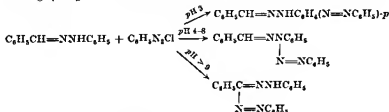
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with hydrazones.¹⁵⁻¹⁸ From the observation that primary hydrazones (IV) couple readily with diazonium salts, whereas secondary hydrazones (V) do not react,¹⁹ he proposed that the first product was an N-azo compound (VI) which rearranged to give the formazan derivative VII.* A crystalline intermediate, assumed to be the N-azo compound, was isolated from the reaction of benzenediazonium chloride with benzaldehyde



phenylhydrazone in alcoholic sodium acetate.¹⁹ Evaporation of an ether solution of this compound produced a formazan.

More recent study of the reaction between benzaldehyde phenylhydrazone and benzenediazonium chloride has shown that the product was dependent on the pH of the reaction medium.^{19a,19b} In a solution of pH 3, benzaldehyde *p*-phenylazophenylhydrazone was isolated. Reaction at pH values of 4 to 8 produced up to 66% yields of 4-benzylidene-1,3-diphenyl-1-tetrazene, whereas at a pH greater than 9 the product was N,N',C-triphenylformazan. The tetrazene changed to the formazan within a few hours at room temperature or rapidly when heated to 90°. Rearrangement also occurred in pyridine or ethanolic potassium hydroxide. The fact that no 1-phenylazo-2-naphthol was formed when the rearrangement was carried out in ethanolic potassium hydroxide containing β -naphthol indicated that the reaction was intramolecular.



¹² Busch and Pfeiffer, *Ber.*, 59, 1163 (1926).

¹⁸ Busch and Schmitt, *Ber.*, **63**, 1950 (1930)

¹⁷ Busch and Schmidt, *J. prakt. Chem.*, [2], 129, 151 (1931).

14. Busch and Schmidt, *J. prakt. Chem.*, [3], 131, 182 (1931).

¹⁸ von Pechmann, Ber., 27, 1672 (1894).

* These compounds are named as derivatives of the hypothetical formazan, $H_2NN=HN=NH$.

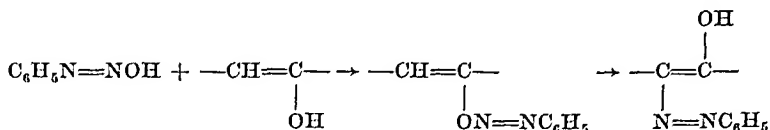
¹⁰⁰ Heintzmann and Périssé, *Experientia*, **10**, 60 (1954) [*C. A.* **49**, 4554 (1955)]

¹⁴⁹ Hauptmann and Périass, *Chem. Ber.*, **89**, 1081 (1956).

structure. It is difficult to establish with certainty the structures in such cases where two tautomeric forms are possible. However, it is generally assumed that the hydrazone is the stable form whenever coupling occurs at a methyl or methylene carbon. Recently, Wiley and Jarboe have presented ultraviolet and infrared absorption data which corroborate this view.^{8b} In the limited number of compounds where coupling occurs on a methinyl carbon without the elimination of a group only the azo structure is possible.

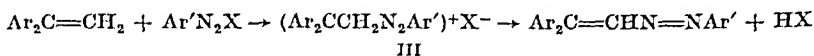
MECHANISMS OF THE REACTIONS

Various mechanisms for the coupling reaction have been proposed. Dimroth observed that reaction occurred only with the enol forms of various ketones.⁹ He proposed that the first product was an enol ether which rearranged to give the final product. The isolation of intermediate



O-azo compounds in certain instances gave further support to his proposal.¹⁰⁻¹² However, these intermediates were isolated only from highly substituted aliphatic reactants such as tribenzoylmethane. It is probable that this mechanism is applicable in special cases.

When certain α,α -diarylethylenes react with diazonium salts, a crystalline intermediate can be isolated.^{13,14} This is considered to be the carbonium salt III. The salt readily loses hydrogen halide to give an



azo compound. Since these intermediates have been isolated only with rather complex molecules, it may be unwise to propose their formation as part of a general mechanism for coupling with all unsaturated hydrocarbons and enols.

Busch has studied the mechanism of the reaction of diazonium salts

^{8b} Wiley and Jarboe, *J. Am. Chem. Soc.*, **77**, 403 (1955).

⁹ Dimroth, *Ber.*, **40**, 2404 (1907).

¹⁰ Dimroth and Hartmann, *Ber.*, **41**, 4012 (1908).

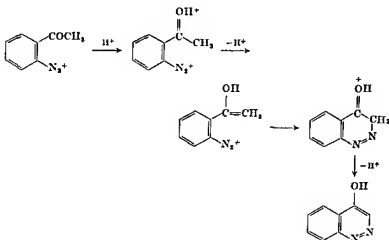
¹¹ Dimroth, Leichtlin, and Friedemann, *Ber.*, **50**, 1534 (1917).

¹² Auwers, *Ann.*, **378**, 243 (1910).

¹³ Diltz and Blankenburg, *J. prakt. Chem.*, [2], **142**, 177 (1935).

¹⁴ Wizinger and Cyriax, *Helv. Chim. Acta*, **28**, 1018 (1945).

Diazotized o-aminoacetophenones also couple intramolecularly with the formation of 4-hydroxycinnolines. This reaction, which is favored by a strongly acidic reaction medium, is believed to proceed through an acid-catalyzed enolization of the carbonyl group.²⁴

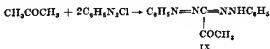


SCOPE AND LIMITATIONS

Since the principal factor that influences this reaction is the nature of the aliphatic reactant rather than that of the diazonium salt, the following discussion is based upon the types of compounds that undergo coupling.

Ketones

Few examples of the reaction of a simple ketone with a diazonium salt have been reported. Acetone reacts with benzenediazonium chloride in alkaline solution to give a product²⁵ that was later identified as methyl formazyl ketone (IX)²⁶. The methyl group in pyruvic acid likewise reacts with two molecules of diazonium salt²⁷. When one of the hydrogen atoms of acetone is replaced by an activating group, the



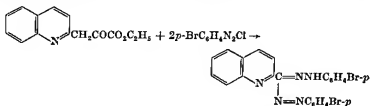
²⁴ Schofield and Simpson, *J. Chem. Soc.*, 1948, 1170

²⁵ Bamberger and Wulz, *Ber.*, 24, 2793 (1891)

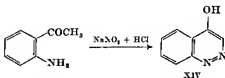
²⁶ von Pechmann, *Ber.*, 25, 3190 (1892)

²⁷ Bamberger and Müller, *Ber.*, 27, 147 (1894)

ethoxalyl group was eliminated when 9-ethoxalylfluorene (XIII) was treated with a diazonium salt.³⁵ The reaction of heterocyclic esters with 2 moles of a diazonium salt is a convenient preparation of C-heterocyclic formazans.³⁶ Ethyl 2-quinolylpyruvate, for example, reacts with *p*-bromobenzenediazonium chloride to give a 79% yield of the formazan.



The only acetophenones that have been shown to undergo coupling are the *o*-aminoacetophenones. When these amines are diazotized, reaction occurs intramolecularly to give 4-hydroxycinnolines. Although this reaction is favored by the presence of electronegative groups ortho or para to the amino group, a 70–75% yield of 4-hydroxycinnoline (XIV) could be obtained by warming a solution of diazotized *o*-aminoacetophenone in hydrochloric acid.³⁷



This transformation proceeds smoothly with a variety of substituted *o*-aminoacetophenones. It has been extended to include *o*-aminophenacyl halides which give 3-halogenated 4-hydroxycinnolines.^{24,38} Higher homologs of *o*-aminoacetophenone produce the corresponding 3-alkyl-4-hydroxycinnolines.^{39–41}

The methylene group in β -diketones reacts readily with diazonium salts. The product may be formulated as the monohydrazone of a triketone. Benzoylacetone, for example, has been converted into the monophenylhydrazone XV in 90% yield.⁴² A variety of β -diketones has been employed in the same general reaction. Cyclic β -diketones, such as

³⁵ Kuhn and Levy, *Ber.*, **61**, 2240 (1928).

³⁶ Rued and Hoffmann, *Ann.*, **581**, 23 (1933).

³⁷ Keneford and Simpson, *J. Chem. Soc.*, 1947, 917.

³⁸ Schofield Swain, and Theobald, *J. Chem. Soc.*, 1949, 2399.

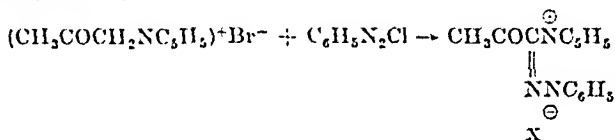
³⁹ Leonard and Boyd, *J. Org. Chem.*, **11**, 419 (1946).

⁴⁰ Keneford and Simpson, *J. Chem. Soc.*, 1948, 334.

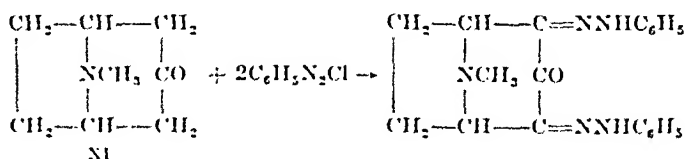
⁴¹ Keneford and Simpson, *J. Chem. Soc.*, 1948, 2318.

⁴² Chattaway and Lye, *J. Chem. Soc.*, 1933, 480.

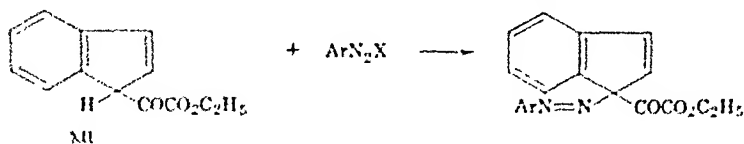
methylene carbon is the one attacked. Compounds of this type that have been investigated include chloroacetone,²⁸ 2,4-dinitrophenylacetone,²⁹ acetonilpyridinium bromide,³⁰ and a variety of 3-acetonil-1,2,4-oxadiazoles.^{31,32} The product from acetonilpyridinium bromide had the betaine structure X.



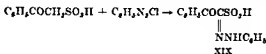
Dieckmann reported that cyclopentane-1,2-dione reacts with benzene-diazonium chloride to give the 1-phenylhydrazone of cyclopentane-1,2,3-trione.³³ The only instance of the coupling of 2 moles of a diazonium salt with a cyclic ketone was the reaction used by Willstätter to show the presence of two active methylene groups in tropinone (XI).³⁴



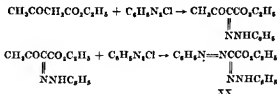
The reaction of a diazonium salt with 1-ethoxalylindene (XII) produces the 1-arylazo compound.³⁵ This contrasts with the observation that the



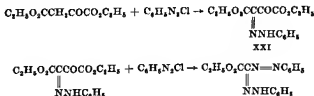
A β -keto sulfonic acid retains the acid group when it couples with a diazonium salt.^{58,59} For example, the phenylhydrazone XIX has been prepared in 60% yield from 2-oxo-2-phenylethane-1-sulfonic acid.



The reactions of β -keto esters with diazonium salts have been studied extensively. Products from ethyl acetoacetate and over fifty different diazonium salts have been reported. Good yields of the α -hydrazones of α,β -diketo esters are obtained if 1 mole of the diazonium salt is employed. However, the use of 2 moles of benzenediazonium chloride causes the elimination of the acetyl group to give an 80% yield of C-carbethoxy-N,N'-diphenylformazan (XX).⁶⁰



Diethyl oxaloacetate likewise can react with 1 or 2 moles of benzenediazonium chloride.⁶¹⁻⁶³ If 1 mole of the salt is used, the product is diethyl dioxosuccinate phenylhydrazone (XXI). The addition of 2 moles of diazonium salt in strongly alkaline solution causes the replacement of the ethoxalyl group



There are no reports of the elimination of groups other than acetyl and ethoxalyl when 2 moles of a diazonium salt react with a β -keto ester

⁵⁸ Parkes and Fisher, *J. Chem. Soc.*, 1936, 83.

⁵⁹ Parkes and Tinsley, *J. Chem. Soc.*, 1934, 1861.

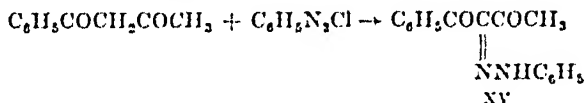
⁶⁰ Bamberger and Wheelwright, *J. prakt. Chem.*, [2], 65, 125 (1902).

⁶¹ Wislicenus and Jensen, *Ber.*, 25, 3443 (1892).

⁶² Rabuchong, *Bull. soc. chim. France*, [3], 31, 76 (1904).

⁶³ Rabuchong, *Bull. soc. chim. France*, [3], 31, 83 (1904).

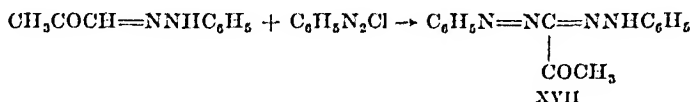
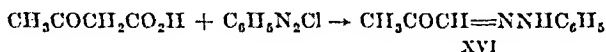
cyclohexane-1,3-dione,⁴³ methone,⁴⁴⁻⁴⁶ and indan-1,3-dione^{47,48} react as readily as the acyclic analogs.



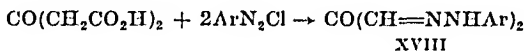
A limited number of β -keto aldehydes has been investigated.⁴⁹⁻⁵¹ In these compounds, the methylene group reacts in the same manner as in β -diketones.

β -Keto Acids, Esters, and Amides

When a β -keto carboxylic acid is treated with a diazonium salt, carbon dioxide is eliminated. The product from the reaction of benzenediazonium chloride with acetonacetic acid is the 1-phenylhydrazone of pyruvaldehyde (XVI). If 2 moles of diazonium salt are employed, methyl formazyl ketone (XVII) is the product.⁵² In carrying out this reaction, the general practice is to saponify a β -keto ester and then to add the diazonium salt solution directly to the hydrolysis mixture without isolation of the unstable β -keto acid.⁵³⁻⁵⁵



Acetonedicarboxylic acid reacts with 2 moles of diazonium salt with the elimination of both carboxyl groups.^{56,57} The resulting product is a mesoxaldehyde diarylhydrazone (XVIII).



⁴³ Vorländer, *Ann.*, **294**, 253 (1897).

⁴⁴ Lifschitz, *Ber.*, **47**, 1401 (1914).

⁴⁵ Iyer and Chakravarti, *J. Indian Inst. Sci.*, **17A**, 41 (1934) [*C. A.*, **28**, 4390 (1934)].

⁴⁶ Iyer, *J. Indian Inst. Sci.*, **21A**, Pt. 6, 65 (1938) [*C. A.*, **33**, 148 (1939)].

⁴⁷ Wislicenus and Reitzenstein, *Ann.*, **277**, 362 (1893).

⁴⁸ Das and Ghosh, *J. Am. Chem. Soc.*, **43**, 1739 (1921).

⁴⁹ Beyer and Claisen, *Ber.*, **21**, 1697 (1888).

⁵⁰ Benary, Meyer, and Charisius, *Ber.*, **59**, 108 (1926).

⁵¹ Benary, *Ber.*, **60**, 914 (1927).

⁵² Bamberger and Lorenzen, *Ber.*, **25**, 3539 (1892).

⁵³ Japp and Klingemann, *J. Chem. Soc.*, **53**, 519 (1888).

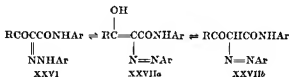
⁵⁴ Japp and Klingemann, *Ann.*, **247**, 190 (1888).

⁵⁵ Reynolds and Van Allan, *Org. Syntheses*, **32**, 84 (1952).

⁵⁶ von Pechmann and Jenisch, *Ber.*, **24**, 3255 (1891).

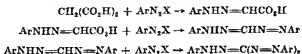
⁵⁷ von Pechmann and Vanino, *Ber.*, **27**, 219 (1894).

pigments. The Hansa Yellows are obtained from the reactions of acetoacetanilides with various diazonium salts.⁶⁷⁻⁶⁹ Many variations in the anilide as well as in the diazonium salt have been studied in attempts to improve the color, stability, and solubility of the resulting dyes. Limitations of space preclude a survey of the extensive patent literature on this subject. However, those β -keto amides whose coupling has been reported in the general literature are included in Table IIC. The dyes may be formulated as existing in both hydrazone (XXVI) and azo (XXVIIa and b) tautomeric forms.

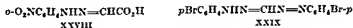


Malonic Acids, Esters, and Amides

Malonic acid can react with 1, 2, or 3 moles of a diazonium salt. It appears that the reaction proceeds through the following steps, with decarboxylation occurring in the first and second stages.⁷⁰ Even when



equimolecular amounts of acid and salt are used, the reaction usually gives a mixture of the first two products. The relative amounts of these substances formed depend upon the nature of the diazonium salt employed. Busch and Wolbring were able to isolate the phenylhydrazone XXVIII in 50% yield from the reaction of malonic acid with *o*-nitrobenzenediazonium chloride, but under similar conditions *p*-bromobenzenediazonium chloride gave mainly *N,N'*-di-(*p*-bromophenyl)formazan



(XXIX).⁷¹ A formazan derivative is the main product with either 1 or 2 moles of most diazonium salts.

⁶⁷ Fierz-David and Ziegler, *Helv. Chim. Acta*, **11**, 776 (1928).

⁶⁸ Burr and Rowe, *J. Soc. Dyers Colourists*, **44**, 205 (1928) [*C. A.*, **22**, 3400 (1928)].

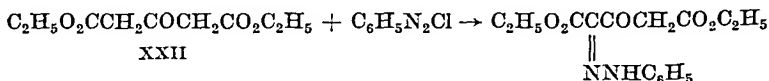
⁶⁹ Rowe, Burr, and Corbushley, *J. Soc. Dyers Colourists*, **42**, 80 (1926) [*C. A.*, **20**, 1715 (1926)].

⁷⁰ von Feckmann, *Ber.*, **25**, 3175 (1892).

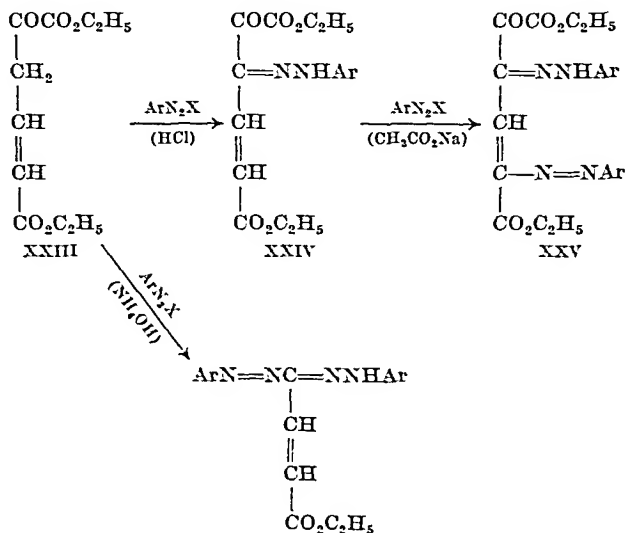
⁷¹ Busch and Wolbring, *J. prakt. Chem.*, [2], **71**, 366 (1903).

containing a methylene group. However, by analogy with the Japp-Klingemann reaction (p. 143), it would be expected that other acyl groups could be eliminated as well.

Diethyl acetonedicarboxylate (XXII) reacts smoothly with 1 mole of diazonium salt.^{64,65} There have been no reports of further reaction with the second methylene group present in the molecule.



Diethyl oxalocrotonate (XXIII) may be regarded as a vinylog of diethyl oxaloacetate. Its behavior with diazonium salts depends upon the pH of the reaction mixture.⁶⁶ When the ester is treated with excess *p*-bromobenzenediazonium chloride in ethanolic hydrochloric acid, the only product is the monophenylhydrazone XXIV. This product is converted into the azo derivative XXV if sodium acetate is added. The original ester reacts with 2 moles of diazonium salt in dilute ammonia with the loss of the ethoxalyl group.

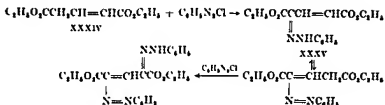


The coupling of diazonium salts with β -keto anilides has been studied extensively, because the products have found use as yellow dyes and

⁶⁴ Balow and Höpfner, *Ber.*, 34, 71 (1901).

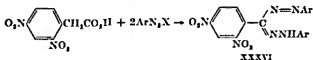
⁶⁵ Balow and Güller, *Ber.*, 44, 2835 (1911).

⁶⁶ Prager, *Ann.*, 338, 360 (1905).

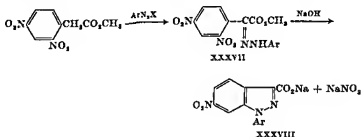


Arylacetic Acids and Esters

The only arylacetic acid that has been observed to couple with diazonium salts is 2,4-dinitrophenylacetic acid.⁷⁷ Decarboxylation occurs as two molecules of the salt attack the α -carbon atom to yield the formazan derivative XXXVI.



Reactions of a variety of diazonium salts with methyl 2,4-dinitrophenylacetate have given good yields of the hydrazones of methyl 2,4-dinitrophenylglyoxalate (XXXVII).^{78,79} These hydrazones undergo ring closure in the presence of alkali with the formation of 1-arylidazoles (XXXVIII).⁷⁸⁻⁸⁰



Although diethyl homophthalate does not react with benzenediazonium chloride, homophthalic anhydride in ethanol-chloroform solution is

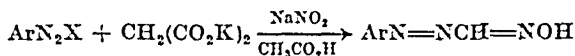
⁷⁷ Parkes and Aldis, *J. Chem. Soc.*, 1938, 1941.

⁷⁸ Borsche and Batschli, *Ann.*, 523, 285 (1936).

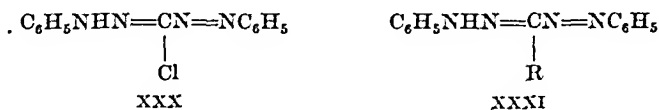
⁷⁹ Borsche and Discont, *Ann.*, 510, 287 (1934).

⁸⁰ Meyer, *Ber.*, 22, 319 (1889).

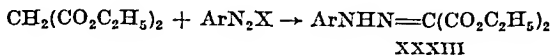
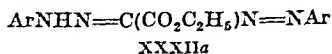
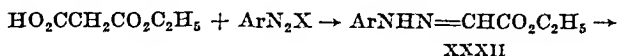
If an acidic solution of a diazonium salt is added to a solution of potassium malonate and sodium nitrite, both nitrosation and coupling take place to yield the azo derivative of formaldoxime.⁷¹



Formazyl chloride (XXX) is obtained from the reaction of 2 moles of benzenediazonium chloride with chloromalononic acid.⁷² Alkylmalonic acids are converted into formazyl alkanes (XXXI) in a similar reaction.⁷³



When malonic acid monoethyl ester reacts with a diazonium salt, carbon dioxide is eliminated with the formation of an arylhydrazone of ethyl glyoxalate (XXXII).^{74a} This hydrazone can react with a second mole of diazonium salt to give the formazan XXXIIa. It appears that the formazan is the only product isolated unless there is an *o*-substituent in the diazonium salt.^{19c,74b} Diethyl malonate, on the other hand, gives the arylhydrazone of diethyl mesoxalate (XXXIII).^{74c} Similarly,



malonamide and its N-substituted derivatives are converted into the hydrazones of the corresponding mesoxalamides.⁷⁵

Diethyl glutaconate (XXXIV) may be regarded as a vinylog of diethyl malonate. Henrich has studied its reactions with both 1 and 2 equivalents of diazonium salt.⁷⁶ The use of 1 equivalent of salt gives diethyl oxoglutaconate phenylhydrazone (XXXV). A second equivalent couples at the other α -carbon atom.

⁷² Fusco and Romani, *Gazz. chim. ital.*, **76**, 419 (1946).

⁷³ Walker, *J. Chem. Soc.*, **123**, 2775 (1923).

^{74a} Leonard, Boyd, and Herbrandson, *J. Org. Chem.*, **12**, 47 (1947).

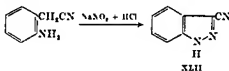
^{74b} S. Parmerter and E. J. Hodges, unpublished observations.

^{74c} Hantzsch and Thompson, *Ber.*, **38**, 2266 (1905).

⁷⁵ Whiteley and Yapp, *J. Chem. Soc.*, **1927**, 521.

⁷⁶ Henrich et al., *Ann.*, **376**, 121 (1910).

Ring closure to give a 71% yield of 3-cyanoindazole (XLII) takes place when *o*-aminophenylacetonitrile is diazotized.⁹⁵ It appears that this cyclization has not been investigated with nuclear-substituted *o*-aminophenylacetonitriles.



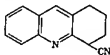
Nitriles in which the cyano group is adjacent to a methinyl carbon vary in their reactions with diazonium salts. Benzylmalononitrile (XLIII),⁹⁶ α -cyano- γ -hydroxybutyric acid lactone (XLIV),⁹⁷ 1,2,3,4-



XLIII



XLIV

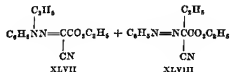
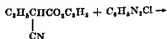


XLV



XLVI

tetrahydroacridine-4-carbonitrile (XLV),⁹⁸ and α -arylsulfonylpropionitriles (XLVI)⁹⁹ form the azo compounds. Ethyl α -cyanobutyrate is reported to undergo two different reactions. With this ester Favrel isolated the hydrazone XLVII formed by migration of the ethyl group,



⁹⁵ Fackhorst and Hoppe, *Ber.*, 43, 2543 (1910).

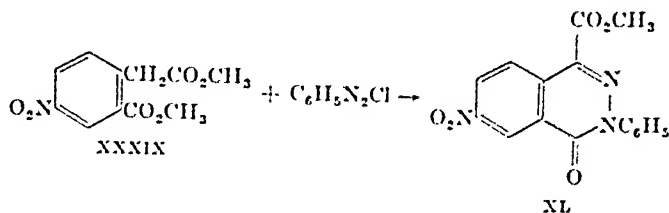
⁹⁶ Curtin and Russell, *J. Am. Chem. Soc.*, 73, 4975 (1951).

⁹⁷ Feofilaktov and Onishchenko, *J. Gen. Chem. U.S.S.R.*, 9, 325 (1939) [*C. A.*, 34, 379

(1940)].

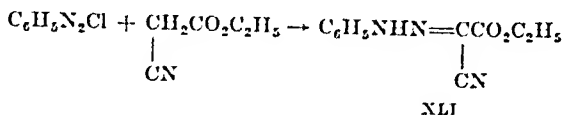
⁹⁸ Borsche and Manteuffel, *Ann.*, 534, 56 (1938).

converted into the α -phenylhydrazono compound.⁸¹ Dimethyl 5-nitrohomophthalate (XXXIX) also couples, and a simultaneous ring closure produces the substituted dihydrophthalazone XL.⁷⁹



Nitriles

A nearly quantitative yield of ethyl cyanoglyoxalate phenylhydrazone (XLI) is obtained from ethyl cyanoacetate and benzenediazonium



chloride in the presence of sodium acetate or sodium carbonate.⁸² A variety of diazonium salts has been used in similar reactions with esters of cyanoacetic acid. Other nitriles that undergo the same type of coupling contain a methylene group between the cyano group and some other activating group. Examples are malononitrile,^{83,84} cyanoacetaldehyde,^{85,86} cyanoacetanilide,^{74a} ethyl cyanopyruvate,^{86,87} nitroacetone,^{88,89} β -iminonitriles,^{90,91} and β -sulfonitriles.^{92,93} The coupling products from β -ketonitriles form chromium complexes that are dyes.⁹⁴ Cyanoacetic acid combines with 2 equivalents of benzenediazonium chloride to produce formazyl cyanide.^{95a}

⁸¹ Dieckmann and Meiser, *Ber.*, **41**, 3253 (1908).

⁸² Krückeberg, *J. prakt. Chem.*, [2], **49**, 321 (1894).

⁸³ Schmidtman, *Ber.*, **29**, 1108 (1896).

⁸⁴ Lythgoe, Todd, and Topham, *J. Chem. Soc.*, **1944**, 315.

⁸⁵ Claisen, *Ber.*, **36**, 3664 (1903).

⁸⁶ Borsche and Manteuffel, *Ann.*, **512**, 97 (1934).

⁸⁷ Fleischhauer, *J. prakt. Chem.*, [2], **47**, 375 (1893).

⁸⁸ Steinkopf and Bohrmann, *Ber.*, **41**, 1044 (1908).

⁸⁹ Steinkopf, *J. prakt. Chem.*, [2], **81**, 193 (1910).

⁹⁰ von Meyer, *J. prakt. Chem.*, [2], **52**, 81 (1895).

⁹¹ von Meyer, *J. prakt. Chem.*, [2], **78**, 497 (1908).

⁹² Tröger and Berndt, *J. prakt. Chem.*, [2], **102**, 1 (1921).

⁹³ Tröger and Wunderlich, *J. prakt. Chem.*, [2], **101**, 157 (1921).

⁹⁴ Long, *J. Am. Chem. Soc.*, **69**, 990 (1947).

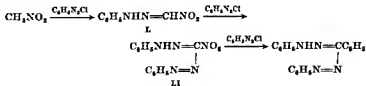
^{95a} Wedekind, *Ber.*, **30**, 2993 (1897).

o-aminophenylsulfonylacetic acid (sulfazone) (XLIXd) and various diazonium salts.¹⁰³



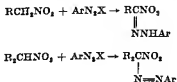
Nitro Compounds

A nitroparaffin that has one or more hydrogen atoms on the α -carbon atom can couple with a diazonium salt. A mixture of products is obtained from the interaction of nitromethane and benzenediazonium chloride¹⁰⁴ Nitroformaldehyde phenylhydrazone (L) is obtained when the reaction is carried out in dilute hydrochloric acid.¹⁰⁵ However, *N,N'*-diphenyl-*C*-nitroformazan (LI) is the principal product in weakly alkaline solution or even at *pH* 4.5.¹⁰ In alkaline solution, a third molecule of diazonium salt causes replacement of the nitro group by a phenyl group.



The product isolated from the reaction of nitromethane with other diazonium salts usually has been the nitroformazan derivative.^{10,106}

Other primary nitroparaffins couple only once to give hydrazones of 1-nitroaldehydes, and secondary nitroparaffins yield azo compounds.



¹⁰³ Claassen, *Ber.*, **45**, 747 (1912)

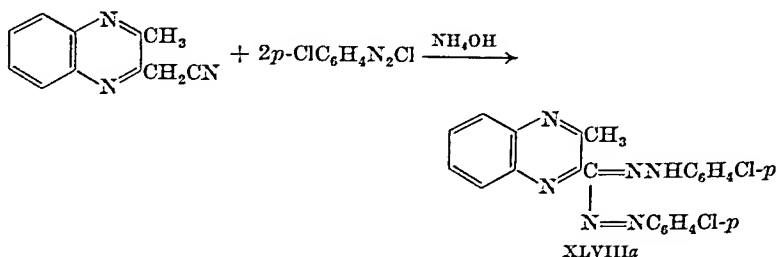
¹⁰⁴ Bamberger, Schmidt, and Levinstein, *Ber.*, **33**, 2043 (1900).

¹⁰⁵ Bamberger, *Ber.*, **27**, 155 (1894)

¹⁰⁶ Hubbard and Scott, *J. Am. Chem. Soc.*, **65**, 2390 (1943).

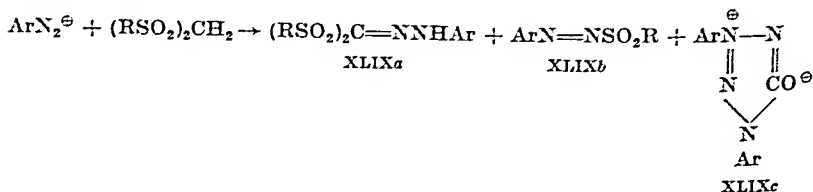
as well as the expected azo compound XLVIII.⁹⁹ When an acetyl group is attached at the methinyl carbon, as in ethyl α -cyanoacetoacetate, the Japp-Klingemann reaction occurs with loss of the acetyl group.¹⁰⁰

One example of the loss of the cyano group during a coupling reaction has been reported.^{36a} The products isolated from the reaction of 3-methylquinoxaline-2-acetonitrile and *p*-chlorobenzenediazonium chloride in dilute ammonium hydroxide were the formazan (XLVIIIa) and urea.



Sulfones

A methylene group adjacent to two sulfonyl groups is attacked by a diazonium salt. The normal product is the monophenylhydrazone XLIXa even when an excess of the salt is used.¹⁰¹ However, in the reaction of *p*-nitrobenzenediazonium fluoroborate with various sulfones two other products, the arylazosulfone XLIXb and the tetrazolium betaine XLIXc, were isolated also.^{10c}



Other sulfones that couple with diazonium salts have a methylene group between a sulfonyl and some other activating group such as nitro,^{19c,102} cyano,^{19c,92,93} carboxyl,^{19c,92} carbethoxy,^{19c,92} or carboxamide.^{19c,92} Claass prepared a series of dyes from the cyclic amide of

⁹⁹ Favrel, *Bull. soc. chim. France*, [4], 47, 1290 (1930).

¹⁰⁰ Favrel, *Bull. soc. chim. France*, [3], 27, 200 (1902).

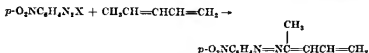
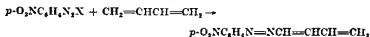
¹⁰¹ Backer, *Rec. trav. chim.*, 70, 733 (1951).

¹⁰² Trüger and Nolte, *J. prakt. chem.*, [2], 101, 136 (1921).

Hydrocarbons

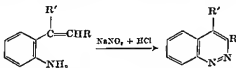
In this section are included aliphatic hydrocarbons and compounds containing a reactive hydrocarbon radical bonded to an aromatic ring

A number of aliphatic hydrocarbons with conjugated double bonds form monoazo derivatives with diazonium salts^{115,116} The yields are usually low, even with the reactive diazonium salts prepared from *p*-nitroaniline or 2,4-dinitroaniline Coupling occurs at the carbon atom having the highest electron density. In 1,3-butadiene this is carbon 1, whereas in 1,3-pentadiene it is carbon 4



The only two monoolefins that couple are 2-methylpropene and 2-methyl-2-butene¹¹⁶ The cyclic hydrocarbons cyclopentadiene^{117,118} and indene¹¹⁹ also give monoazo derivatives.

The coupling of α,α -diarylethylenes with diazonium salts was discussed above (p. 4). A similar reaction, which occurs intramolecularly when *o*-aminophenylethylenes are diazotized, is the Widman-Stoermer synthesis of cinnolines.¹¹⁹⁻¹²¹ The scope of this reaction has been studied by



Simpson and Stephenson,¹²² and by Schofield,¹²³ who have found that good yields of the cinnoline are obtained when R' is methyl or aryl and R is hydrogen. Cinnoline formation also occurs when both R and R' are aromatic. However, if R' is hydrogen or carboxyl and R is aromatic,

¹¹⁵ Meyer, *Ber.*, 52, 1468 (1919)

¹¹⁶ Terent'ev and Demidova, *J. Gen. Chem. U.S.S.R.*, 7, 2464 (1937) [*C. A.*, 32, 2094 (1938)].

¹¹⁷ Eibner and Laue, *Ber.*, 39, 2022 (1906)

¹¹⁸ Terent'ev and Gomborg, *J. Gen. Chem. U.S.S.R.*, 8, 662 (1938) [*C. A.*, 33, 1285 (1939)].

¹¹⁹ Widman, *Ber.*, 17, 722 (1884).

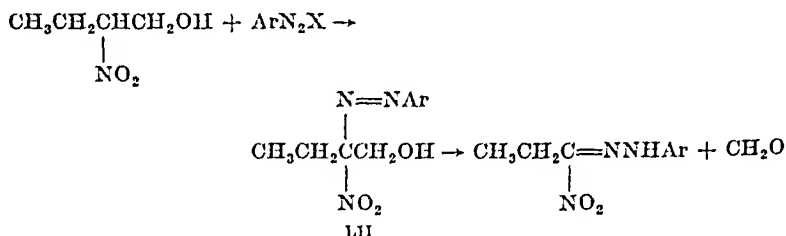
¹²⁰ Stoermer and Fincke, *Ber.*, 42, 3115 (1909)

¹²¹ Stoermer and Gauss, *Ber.*, 45, 3104 (1912).

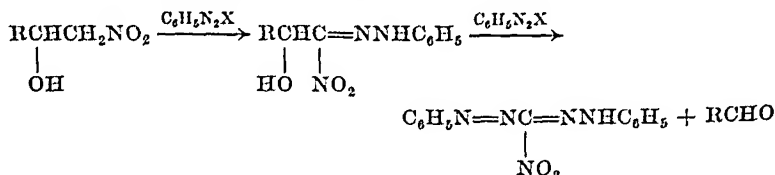
¹²² Simpson and Stephenson, *J. Chem. Soc.*, 1942, 353

¹²³ Schofield, *J. Chem. Soc.*, 1949, 2408

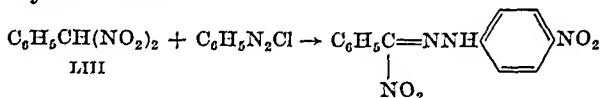
Degradation of the molecule sometimes occurs when a nitroalcohol reacts with a diazonium salt. For example, 2-nitropropanol and benzene-diazonium chloride give formaldehyde and a 78% yield of 1-nitroacetaldehyde phenylhydrazone.¹⁰⁷ Similarly, 2-nitro-1-butanol is converted into 1-nitropropionaldehyde phenylhydrazone. If the reaction mixture from 2-nitro-1-butanol and a diazonium salt is acidified immediately, the



2-aryldiazo-2-nitro-1-butanol (LII) can be isolated.¹⁰⁸ 2-Hydroxy-1-nitroparaffins couple normally to give the phenylhydrazones of 2-hydroxy-1-nitroaldehydes. However, the addition of a second mole of diazonium salt causes the elimination of aldehyde from these products.¹⁰⁷



Migration of the nitro group is observed when the α -carbon atom holds two other electron-attracting substituents, one of which is a phenyl group. In these instances the nitro group migrates to the position para to the hydrazone group. (If the para position is blocked, the nitro group enters the ortho position.) Examples that have been reported include phenyldinitromethane (LIII),¹⁰⁹⁻¹¹¹ diphenylnitromethane,^{112,113} and α -nitrophenylacetonitrile.¹¹⁴



¹⁰⁷ Jones and Kenner, *J. Chem. Soc.*, 1930, 919.

¹⁰⁸ Gochenour and Degering, *Proc. Indiana Acad. Sci.*, 57, 88 (1948) [*C. A.*, 43, 4046 (1949)].

¹⁰⁹ Ponzio, *Gazz. chim. ital.*, 39, II, 535 (1909).

¹¹⁰ Ponzio and Macciotta, *Gazz. chim. ital.*, 44, I, 269 (1914).

¹¹¹ Ponzio and Macciotta, *Gazz. chim. ital.*, 44, II, 63 (1914).

¹¹² Ponzio, *Gazz. chim. ital.*, 42, I, 525 (1912).

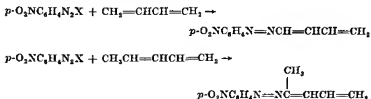
¹¹³ Busch and Schäffner, *Ber.*, 56, 1612 (1923).

¹¹⁴ Ponzio and Giovetti, *Gazz. chim. ital.*, 39, II, 546 (1909).

Hydrocarbons

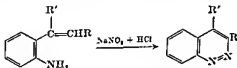
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¹¹⁵ Meyer, *Ber.*, 52, 1468 (1919).

¹¹⁶ Terent'ev and Demidova, *J. Gen. Chem. U.S.S.R.*, 7, 2464 (1937) [*C. A.*, 32, 2094 (1938)].

¹¹⁷ Fibner and Laue, *Ber.*, 39, 2022 (1906).

¹¹⁸ Terent'ev and Gomborg, *J. Gen. Chem. U.S.S.R.*, 8, 662 (1939) [*C. A.*, 33, 1245 (1939)].

¹¹⁹ Widman, *Ber.*, 17, 722 (1884).

¹²⁰ Stoermer and Fincke, *Ber.*, 42, 3115 (1909).

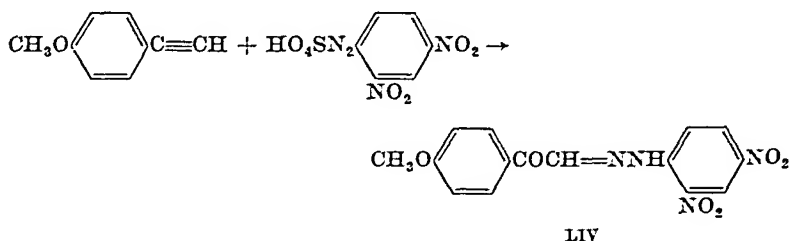
¹²¹ Stoermer and Gaus, *Ber.*, 45, 3104 (1912).

¹²² Simpson and Stephenson, *J. Chem. Soc.*, 1942, 353.

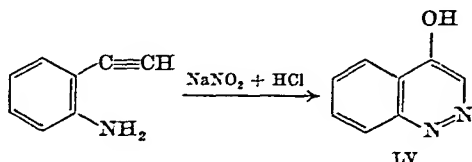
¹²³ Schofield, *J. Chem. Soc.*, 1949, 2404.

the diazotized amine undergoes the Pschorr reaction to yield a phenanthrene derivative.

When *p*-methoxyphenylacetylene couples with 2,4-dinitrobenzene-diazonium sulfate, a 69% yield of α -*p*-anisylglyoxal β -2,4-dinitrophenylhydrazone (LIV) is formed.¹²⁴ This reaction is similar to the synthesis



of 4-hydroxycinnoline (LV) from diazotized *o*-aminophenylacetylene.¹²⁵ In each case the elements of a hydroxyl group, derived from the aqueous reaction medium, appear in the product. This ring closure was used first



by von Richter to make 4-hydroxycinnoline-3-carboxylic acid from *o*-aminophenylpropionic acid.¹²⁶ Recent examples of the reaction have employed nuclear substituted *o*-aminophenylacetylenes, *o*-aminophenylpropionic acids, and *o*-aminodiphenylacetylene.^{23,125}

Although styrene does not react with 2,4-dinitrobenzenediazonium sulfate, *p*-methoxystyrene (LVI) is converted to the 2,4-dinitrophenylhydrazone of anisaldehyde by this reagent.¹²⁴ The same product is obtained when the dry diazonium salt is added to an alcoholic solution of anethole (LVII).¹²⁷ Acetaldehyde is eliminated in the second reaction. Other compounds that show a similar coupling with the loss of acetaldehyde are isoeugenol,¹²⁸ isosafrole,¹²⁷ isopairole,¹²⁷ and *p*-propenyl-dimethylaniline.¹²⁹ It is even possible to obtain a 60% yield of *p*-hydroxybenzaldehyde *p*-nitrophenylhydrazone from the action of dry

¹²⁴ Ainley and Robinson, *J. Chem. Soc.*, 1937, 369.

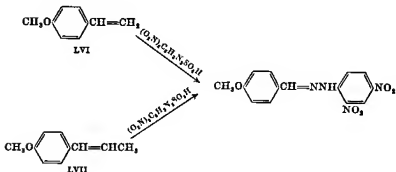
¹²⁵ Schofield and Simpson, *J. Chem. Soc.*, 1945, 512.

¹²⁶ von Richter, *Ber.*, 16, 677 (1883).

¹²⁷ Quilico and Freri, *Gazz. chim. ital.*, 58, 390 (1928).

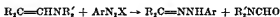
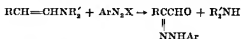
¹²⁸ Quilico and Fleischner, *Gazz. chim. ital.*, 59, 39 (1929).

¹²⁹ Quilico and Freri, *Gazz. chim. ital.*, 60, 606 (1930).

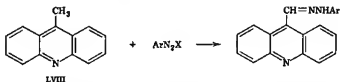


p-nitrobenzenediazonium sulfate on an alcoholic solution of *p*-propenylphenol.¹³⁰

The reaction of an α,β -unsaturated tertiary amine with a diazonium salt resembles that of an unsaturated hydrocarbon. Coupling occurs at the β -carbon atom, and the amino group is eliminated. If there is a hydrogen substituent on the β -carbon, the β -arylhydrazone of a glyoxal is obtained. However, if there is no hydrogen attached to the β -carbon, the enamine is cleaved to give the hydrazone of a ketone.^{130a}



Methyl groups in the α or γ positions of some heterocyclic compounds combine with diazonium salts. For example, 9-methylacridine (LVIII)



has been coupled with a number of salts to give the arylhydrazones of acridine 9-carboxaldehyde.¹³¹ If the hetero atom is converted into the onium salt, the activity of the methyl group is increased.¹³² 2,3,3-Trimethylindolenine is an exception, for the base is more reactive than

¹³⁰ Quilico and Freri, *Gazz. chim. ital.*, 59, 600 (1929).

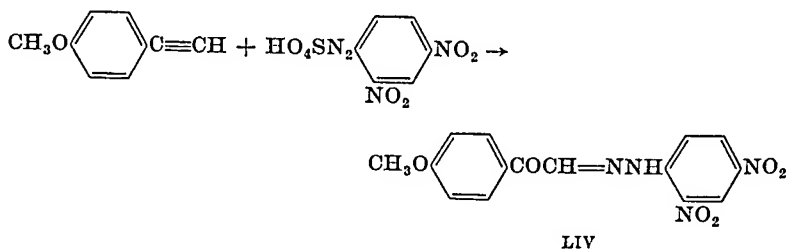
^{130a} Cray, Quayle, and Lester, *J. Am. Chem. Soc.*, 78, 5584 (1956).

¹³¹ Porai Koshits and Kharkharov, *Bull. acad. sci. U.R.S.S. classe sci. chim.*, 1944, 143 [*C. A.*, 39, 1631 (1945)].

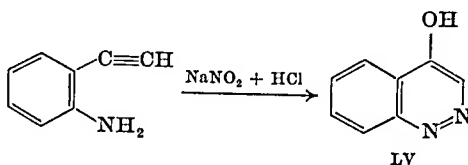
¹³² Kharkharov, *J. Gen. Chem. U.S.S.R.*, 23, 1175-1181 (1953) [*C. A.*, 47, 12390 (1953)].

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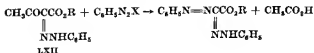
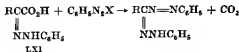
¹²⁷ Quilico and Freri, *Gazz. chim. ital.*, 58, 380 (1928).

¹²⁸ Quilico and Fleischner, *Gazz. chim. ital.*, 59, 39 (1929).

¹²⁹ Quilico and Freri, *Gazz. chim. ital.*, 60, 606 (1930).

not take place with secondary hydrazones was mentioned on p 5.¹⁹ The reaction of the phenylhydrazones of 2-hydroxy-1-nitroaldehydes with degradation of the molecule to give an aldehyde and nitroformazan was mentioned under the discussion of nitro compounds. The formazans obtained from phenylhydrazones of aldoses have proved to be useful derivatives of these sugars^{139a-f}

The hydrazones of only two kinds of ketones have been converted into formazans. These are the arylhydrazones of α -keto acids (LXI)^{19,140-145} and the α -arylhydrazones of α,β -diketobutyric esters (LXII).^{19,60,142,146} With the first type coupling causes decarboxylation, and with the second type an acetyl group is replaced. These eliminations are very similar to the Japp-Klingemann reaction.



Reports of the isolation of two isomeric forms of unsymmetrical formazans^{146,147} have been shown to be erroneous¹⁴⁸⁻¹⁵⁰ The unsymmetrical formazans obtained by both possible routes (A and B) are identical. The isolation of the same compound from both of these reactions has been rationalized by the assumption that the product has the structure of the resonance hybrid of the chelated forms LXIII^{146,149}

^{139a} Mester, *J Am Chem. Soc.*, **77**, 4301 (1955)

^{139b} Mester and Major, *J Am Chem Soc.*, **78**, 1403 (1956).

^{139c} Zemplén and Mester, *Acta Chim Acad Sci Hung.*, **2**, 9 (1952) [*C A.*, **43**, 1966 (1954)].

^{139d} Mester and Major, *J Am Chem. Soc.*, **77**, 4305 (1955).

^{139e} Mester and Major, *J. Am. Chem. Soc.*, **77**, 4297 (1955).

^{139f} Zemplén, Mester, Messmer, and Eckhart, *Acta Chim Acad Sci Hung.*, **2**, 25 (1952) [*C A.*, **43**, 1966 (1954)]

¹⁴⁰ Bamberger, *Ber.*, **25**, 3547 (1892)

¹⁴¹ Wedekind and Stauwe, *Ber.*, **31**, 1746 (1898)

¹⁴² Bamberger and de Gruyter, *J prakt Chem.*, [2], **64**, 222 (1901).

¹⁴³ Busch and von Beust, *Ber.*, **58**, 442 (1925)

¹⁴⁴ Ragno and Bruno, *Gazz. chim. ital.*, **76**, 485 (1946).

¹⁴⁵ Fusco and Romani, *Gazz. chim. ital.*, **78**, 342 (1948).

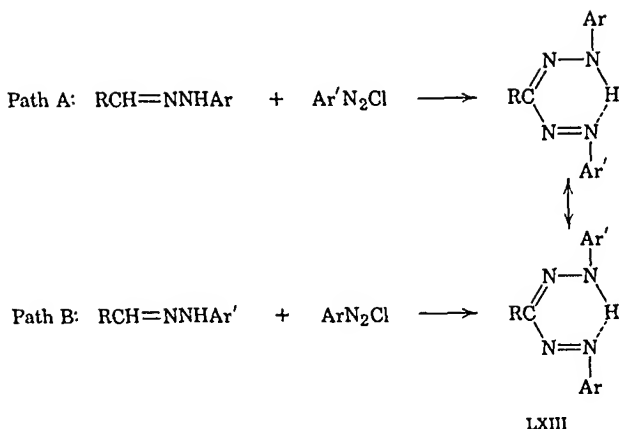
¹⁴⁶ Lapworth, *J. Chem. Soc.*, **83**, 1114 (1903)

¹⁴⁷ Fichter and Schuess, *Ber.*, **33**, 747 (1900)

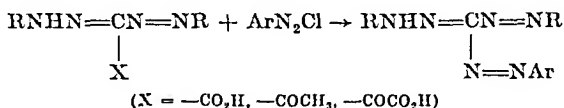
¹⁴⁸ Kuhn and Jerchel, *Ber.*, **74**, 941 (1941).

¹⁴⁹ Hunter and Roberts, *J Chem Soc.*, **1941**, 820.

¹⁵⁰ Hausner, Jerchel, and Kuhn, *Chem Ber.*, **84**, 651 (1951).



A formazan in which the carbon is joined to a carboxyl,^{19,70,140,151,152} acetyl,^{52,142} or oxalyl group¹⁵³ loses that group when it couples with another molecule of diazonium salt.



Heterocyclic Compounds

In this section are included those heterocyclic compounds that have a methylene group with a carbonyl group adjacent to it in the ring. These reactants can exist in the tautomeric enolic form as well.

Of the compounds in this group, the 5-pyrazolones have been investigated most extensively because of the successful use of their azo derivatives as dyes. No attempt has been made to include here all of the pyrazolones that appear in the patent literature. The early patents in this field have been reviewed by Roux and Martinet,¹⁵⁴ and some of the more recent ones have been discussed by Venkataraman.¹⁵⁵ The 1-aryl-3-methyl-5-pyrazolones (LXIV) have been used most frequently in the preparation of dyes. Pyrazolones with a methyl group in the

¹⁵¹ Bamberger and Wheelwright, *Ber.*, **25**, 3201 (1892).

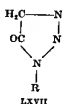
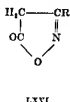
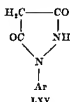
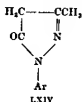
¹⁵² Chattaway and Lye, *Proc. Roy. Soc. London*, **A137**, 489 (1932) [*C. A.*, **26**, 5555 (1932)].

¹⁵³ Bamberger and Muller, *J. prakt. Chem.*, [2], **64**, 190 (1901).

¹⁵⁴ Roux and Martinet, *Rev. gén. mat. color.*, **27**, 115-120, 134-139, 152-155 (1923), **28**, 13-14, 74-77 (1924).

¹⁵⁵ Venkataraman, *The Chemistry of Synthetic Dyes*, Chapter XVIII, Academic Press, New York, 1952.

4-position fail to react with diazonium salts¹⁵⁶ On the other hand, pyrazolones with an ethylene, isopropylidene, or benzal group in the 4-position couple with the loss of that substituent.^{157,158}



Other heterocycles that contain a methylene group active toward diazonium salts include 3,5-pyrazolidinediones (LXV), 5-isoxazolones (LXVI), 1,2,3-triazole 5-ones (LXVII), 2(3)-thianaphthenone (LXVIII), 3(2)-thianaphthenone (LXIX), 1-phenyloxindole (LXX), indoxyl (LXXI), barbituric acid, and homophthalimide.



SYNTHETIC APPLICATIONS

The reactions of diazonium salts with many aliphatic compounds have been used only to prepare derivatives for purposes of characterization. The adaptability of the reaction to large-scale syntheses is evident from the quantities of dyes that have been produced from β -ketoamides and 5-pyrazolones. The Pschorr synthesis and related diazonium ring closure reactions are discussed in Chapter 7 of *Organic Reactions*, Volume 9.

Cinnolines

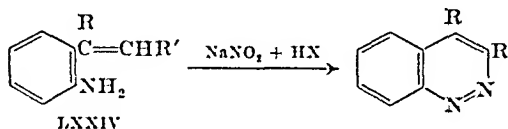
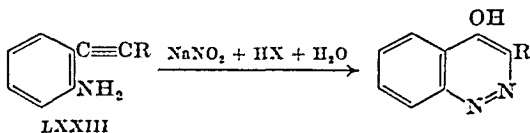
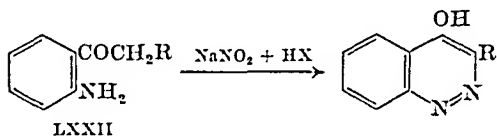
All of the general methods for the preparation of cinnolines employ the intramolecular coupling of a diazonium salt with some aliphatic substituent

¹⁵⁶ Verkade and Dhont, *Rec. trav. chim.*, **64**, 165 (1945)

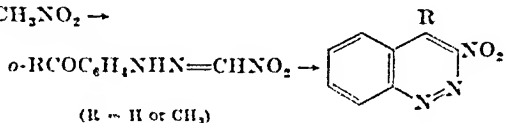
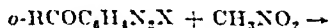
¹⁵⁷ Stolz, *Ber.*, **28**, 623 (1895)

¹⁵⁸ Sawdey, Ruoff, and Vittum, *J. Am. Chem. Soc.*, **72**, 4947 (1950)

in the ortho position. The Borsche synthesis¹⁵⁹ from *o*-aminophenyl ketones (LXXII) has been used to prepare a variety of 3-, 5-, 6-, 7-, and 8-substituted 4-hydroxycinnolines.^{22,24,37-41,159-167a,b} The method of von Richter¹²⁶ based upon *o*-aminophenylacetylenes (LXXIII) produces 3-carboxy- or 3-phenyl-4-hydroxycinnolines.^{23,125} Cinnolines with alkyl or aryl substituents in the 4 position are obtained by the Widman-Stoermer synthesis from *o*-aminoarylethylenes (LXXIV).^{119-121,167c}



3-Nitrocinnolines have been synthesized by coupling diazotized *o*-aminobenzaldehyde or *o*-aminoacetophenone with nitromethane and cyclizing the resulting arylhydrazone of nitroformaldehyde.^{167d}

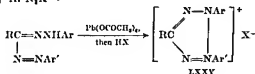
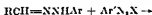


Indazoles

Intramolecular coupling of diazotized *o*-toluidines has been used to prepare a number of substituted indazoles. This method is best for the synthesis of nitroindazoles (LIX). A good yield of indazole-3-carboxylic acid is obtained via the nitrile XLII from *o*-aminophenylacetonitrile.^{155,166} A method for the preparation of 1-aryl-6-nitroindazoles (XXXVIII) employs the reaction of a diazonium salt with methyl 2,4-dinitrophenylacetate. When the resulting hydrazone is treated with alkali, it undergoes ring closure with the loss of one nitro group.⁷⁴⁻⁸⁰

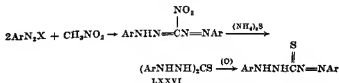
Tetrazolium Salts

When a formazan is oxidized with lead tetraacetate, a tetrazolium salt (LXXV) is produced. The formazans in turn are synthesized by coupling a diazonium salt with an arylhydrazone. This general route appears to be the only good one for the preparation of tetrazolium salts. The preparations and uses of formazans and tetrazolium salts have been reviewed by Ried¹⁶⁷ and by Nineham.¹⁶⁸



Thiocarbazones

The first step in the synthesis of thiocarbazones utilizes the reaction of nitromethane with two equivalents of diazonium salt.^{169,166,170} The resulting nitroformazan is reduced by ammonium sulfide to the thio-carbazide LXXVI which is oxidized readily to the thiocarbazone.

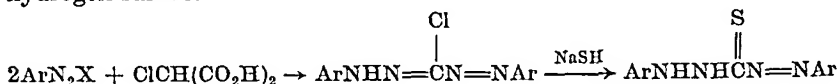


¹⁶⁶ Rousseau and Lindwall, *J. Am. Chem. Soc.*, **72**, 3047 (1950).

¹⁶⁷ Ried, *Angew. Chem.*, **64**, 391 (1952); Nineham, *Chem. Revs.*, **55**, 355 (1955).

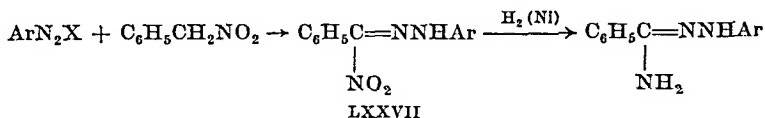
¹⁶⁸ Osaper and Klungenberg, *J. Org. Chem.*, **13**, 309 (1948).

A related synthesis starts with chloromalononic acid.^{170a} In this method the chloroformazan is converted directly to the thiocarbazone by sodium hydrogen sulfide.



Amidrazones*

The catalytic reduction of arylhydrazones of α -nitrobenzaldehyde (LXXVII) offers a convenient synthesis of amidrazones.¹⁷¹ Coupling of a diazonium salt with phenylnitromethane furnishes the required hydrazone. Ponzio obtained the amidrazones from the reaction of the α -nitrobenzaldehyde arylhydrazone with ammonia.¹⁷²



Amines

The only report of the use of the coupling reaction to introduce the amino group into active methylene compounds appears in the patent literature.¹⁷³ In this method the phenylhydrazones obtained from ethyl acetoacetate, ethyl cyanoacetate, or acetylacetone and benzenediazonium chloride were reduced with zinc and acetic acid to give the α -acetamido compounds.

EXPERIMENTAL CONDITIONS

Diazonium salts react with so many different types of aliphatic compounds that it is difficult to make generalizations about experimental conditions. However, the following summary may serve as a useful guide.

Diazonium Salts

For the diazotization of most arylamines a solution of sodium nitrite is added to a cold solution of the arylamine in aqueous mineral acid.

^{170a} Irving and Bell, *J. Chem. Soc.*, 1953, 3538.

* Amidrazones may be represented by the general formula $\text{RC}(\text{NH}_2)=\text{NNHR}'$. They are indexed in *Chemical Abstracts* as the hydrazones of amides.

¹⁷¹ Jerchel and Fischer, *Ann.*, 574, 85 (1951).

¹⁷² Ponzio, *Gazz. chim. ital.*, 40, I, 312 (1910).

¹⁷³ Pfister and Tishler, U.S. pat. 2,480,927 [*C. A.*, 44, 2552 (1950)].

For weakly basic amines or amino acids it is necessary to employ special techniques. These methods have been reviewed by Saunders.¹⁷⁴

Solvents

These reactions have been conducted most frequently in cold dilute aqueous solutions buffered with sodium acetate. Alcohol or occasionally pyridine or acetic acid is added if the reactants are too insoluble in water. Special reactions that have been carried out under anhydrous conditions were discussed under Scope and Limitations, pp. 22-23.

pH

Reaction can occur between a diazonium salt and many active methylene compounds over a wide pH range. Coupling in dilute hydrochloric acid^{64,82} or in dilute sodium hydroxide¹⁷⁵ is usually less satisfactory than coupling in the presence of sodium carbonate or sodium acetate buffers.⁸² The general practice is to use a large excess of sodium acetate.

Hunig and Boes made an extensive study of the relative reactivity of various methylene compounds, XCH_2Y , toward *p*-nitrobenzenediazonium fluoroborate over a pH range from 2 to 10.¹⁸⁶ The lowest pH at which a compound would couple was taken as an indication of its reactivity. The substituents X and Y arranged in the order of their decreasing ability to activate were. NO_2 , CHO, $COCH_3$, CN, $CO_2C_2H_5$, $CONH_2$, CO_2CH_3 , $SO_2C_2H_5$, $SOCH_3$, C_6H_5 . Only the most active compounds coupled in acidic solution, and the least active failed to couple even in alkaline solution.

In the intramolecular coupling reactions used to prepare cinnolines or indazoles a strongly acidic solution is employed. This promotes the coupling reaction and decreases the competing decomposition of the diazonium salt to the phenol. Acidic solutions are used in the reactions of diazonium salts with hydrocarbons for similar reasons.

The optimum reaction conditions for nitro compounds vary considerably. It has been customary to employ an aqueous solution of the sodium salt of the *aci*-nitro compound. The coupling of nitromethane, on the other hand, proceeds well at a pH of 4.5.⁸² With nitro alcohols a fairly high pH is required. The reaction of 2-nitro-1-butanol with *p*-chlorobenzenediazonium chloride does not occur below pH 10.8, and best yields are obtained at pH 13.9.¹⁸⁸ It has been reported that solutions

¹⁷⁴ Saunders, *The Aromatic Diazo Compounds*, Edward Arnold & Co., London, 1949.

¹⁷⁵ von Rothenburg, *Ber.*, **27**, 685 (1894)

of 1-N-morpholino-2-nitropropane between pH 7 and 10 *explode with great violence during the coupling process*.¹⁷⁵²

Reactant Ratios

Equivalent amounts of reactant and diazonium salt are most commonly employed. Excess diazonium salt should be avoided since the product is frequently a hydrazone which can couple with another molecule of the salt to produce a formazan derivative. The latter reaction is favored by a strongly alkaline solution.

Time of the Reaction

Since most of the coupling reactions are rapid, the product can be isolated soon after the diazonium salt has been added. However, the reactions that involve intramolecular coupling require more time for completion. In the preparation of indazoles, the diazotized *o*-toluidine derivative may be left for several days to effect the ring closure.^{127,128} Likewise, the formation of cinnolines is often slow.^{22,23,24,154-157-4} For certain cinnolines this cyclization is accelerated by the use of a warm, strongly acidic reaction medium.^{27,49}

EXPERIMENTAL PROCEDURES

The preparation of pyruvaldehyde 1-phenylhydrazone from acetoacetic acid and benzenediazonium chloride in 73-82% yield is described in *Organic Syntheses*.⁵⁵

Directions for the preparation of 5-nitroindazole in yields of 72-89% by the intramolecular coupling of diazotized 2-methyl-4-nitroaniline are given in *Organic Syntheses*.¹²⁸

room temperature One liter of water is added before the yellow solid is collected The yield is 229 g. (98%) of product that melts at about 70°, but whose melting point varies markedly with the rate of heating.

Ethyl Cyanoglyoxalate *m*-Chlorophenylhydrazone.¹⁴⁰ A solution of 38 g (0.30 mole) of *m*-chloroaniline in 85 ml. of concentrated hydrochloric acid and 300 ml. of water is cooled to 5° with stirring. Diazotization is effected by the slow addition of a solution of 23 g. (0.33 mole) of sodium nitrite in 50 ml. of water while the temperature is held below 5°. The solution is stirred with activated carbon for an additional ten minutes (temperature below 10°) and filtered. The filtrate is added dropwise during one hour to a well-stirred mixture of 33.9 g (0.30 mole) of ethyl cyanoacetate in 300 ml of water at 5–10°. Sodium carbonate (100 g) is added in small portions to keep the mixture alkaline to litmus. The mixture is extracted with ether until the extracts are no longer colored. The combined ether extracts are dried over magnesium sulfate and concentrated. The residue is crystallized from ethanol to give 73 g. (97%) of pale-orange crystals, m p. 89–90°.

By the same procedure, diethyl malonate is converted into diethyl mesoxalate *m*-chlorophenylhydrazone in 78% yield. Likewise, ethyl acetoacetate is converted into ethyl α,β -dioxobutyrate α -*m*-chlorophenylhydrazone in 78% yield.

1-Nitro-1-*p*-chlorophenylhydrazonoethane.¹⁴⁰ To a cold solution of 8.4 g. (0.066 mole) of *p*-chloroaniline in 17 ml of concentrated hydrochloric acid and 200 ml of water is added slowly with stirring a solution of 4.7 g (0.068 mole) of sodium nitrite in 50 ml. of water. The temperature is held at 0–5° during the addition. After ten minutes, the solution is diluted with 1.7 l. of cold water, and 30 g. of sodium acetate trihydrate is added. Meanwhile, 5 g. (0.066 mole) of nitroethane is dissolved in an ice-cold solution of 2.6 g of sodium hydroxide in 20 ml. of water. The nitroethane solution is added dropwise during ten minutes to a well-stirred solution of the diazonium salt. The temperature of the mixture is held at 5–10° during the addition. After thirty minutes the orange solid is collected. The yield of product melting at 116–118° is 14 g. (100%). Recrystallization from ethanol gives orange-yellow crystals which decompose at 126–127° when placed in a bath preheated to 120°.

1-(*p*-Nitrophenylazo)-2,3-dimethyl-1,3-butadiene.¹¹⁵ A warm solution of 13.8 g. (0.10 mole) of *p*-nitroaniline in 25 ml of concentrated hydrochloric acid and 25 ml. of water is poured onto 100 g of ice. The mixture is stirred with a solution of 7 g (0.10 mole) of sodium nitrite in 50 ml of water until the solid dissolves. The solution is diluted with 100 ml. of water and shaken for two hours with 9 g. (0.11 mole) of

¹⁴⁰ Bamberger and Grob, *Ber.*, 25, 67 (1902)

2,3-dimethyl-1,3-butadiene.^{176c} The solid is collected and dried to give 12 g. (47%) of product. After recrystallization from acetic acid containing some charcoal, the product melts at 177°.

N,N'-Diphenyl-C-methylformazan.¹³⁹ Aqueous benzenediazonium chloride is prepared by the addition of a solution of 7 g. (0.1 mole) of sodium nitrite in 15 ml. of water to 9.3 g. (0.1 mole) of aniline dissolved in 25 ml. of concentrated hydrochloric acid and 25 ml. of water. A warm solution of 13.4 g. (0.1 mole) of acetaldehyde phenylhydrazone (α or β form) in 100 ml. of ethanol is mixed with a warm solution of 30 g. of sodium acetate trihydrate in 150 ml. of ethanol. The mixture is cooled to 5° with vigorous stirring before the diazonium salt solution is added dropwise. The product separates as an oil which soon solidifies. The solid is collected and washed with a little cold ethanol to give 21 g. (88%) of N,N'-diphenyl-C-methylformazan, which melts at 123°. Recrystallization from ethanol raises the melting point to 125°.

4-Hydroxy-3-methylcinnoline.⁴⁰ To a cold solution of 45.5 g. (0.31 mole) of *o*-aminopropiophenone in 1.2 l. of concentrated hydrochloric acid is added slowly with stirring 23 g. (0.33 mole) of sodium nitrite in 30 ml. of water. The temperature is kept at 5–10° during the addition. The solution is filtered, and 4 l. of concentrated hydrochloric acid is added to the filtrate. The reaction mixture is warmed at 60° for four hours before it is evaporated to a small volume under reduced pressure. An excess of saturated sodium acetate solution is added to precipitate the product, which is collected and dried to give 40.7 g. (83%) of almost pure 4-hydroxy-3-methylcinnoline. Recrystallization from 50% aqueous ethanol gives slender, silvery needles, m.p. 241–242°.

TABULAR SURVEY OF THE COUPLING OF DIAZONIUM SALTS WITH ALIPHATIC CARBON ATOMS

The tables include those reactions recorded prior to the January, 1956, issue of *Chemical Abstracts*. Some more recent examples are also given. The reactants within a table are in general listed in order of increasing size and complexity.

Where more than one reference is given for a single entry, the yield reported is taken from the first reference. Since yields are but infrequently reported, the omission of parenthesized figures in the product column indicates that no yield was reported:

^{176c} Allen and Bell, *Org. Syntheses Coll.* Vol. 3, 312 (1955).

TABLE I

COUPLING OF DIAZONIUM SALTS WITH KETONES

A. Monoketones

Ketone	Substituent(s) in Aniline*	Product (Yield, %)	References
Acetone	—	$C_6H_5NHN=C(COCH_3)_2N=NC_6H_5$	25
Chloroacetone	—	$CH_3COC(Cl)=NNHC_6H_5$ (30)	28
	2-Methyl	$CH_3COC(Cl)=NNHC_6H_4CH_3-o$ (25)	28
	4-Methyl	$CH_3COC(Cl)=NNHC_6H_4CH_3-p$ (15)	28
α,α' -Dichloroacetone	—	$ClCH_2COC(Cl)=NNHC_6H_5$	177
	2-Methyl	$ClCH_2COC(Cl)=NNHC_6H_4CH_3-o$	177
	4-Methyl	$ClCH_2COC(Cl)=NNHC_6H_4CH_3-p$	177
α,α' -Dichloroacetone	—	$(C_6H_5N=N)_2CCl_2$	177
	4-Methyl	$(p-CH_3C_6H_4N=N)_2CCl_2$	177
sym -Tetrachloroacetone	—	$(C_6H_5N=N)_2CCl_2$	177
	4-Methyl	$(p-CH_3C_6H_4N=N)_2CCl_2$	177
Nitroacetone	4-Nitro	$CH_3COC(NO_2)=NNHC_6H_4NO_2-p$ (59)	19c
Methylsulfonylacetone	4-Nitro	$CH_3SO_2C(COCH_3)=NNHC_6H_4NO_2-p$ (70)	19c
4-Imino-2-pentanone	—	$CH_3COC(COCH_3)=C(NH_2)CH_3$	178
Pyruvic acid	—	$C_6H_5NHN=C(N=NC_6H_5)COCO_2H$ (57)	153, 227
Levulinic acid	—	Diormazy† (88)	179, 153, 180
γ -Oxopimelic acid	—	Diormazy†† (13-17)	153, 180
Cyclopentane-1,2-dione	—	Cyclopentane-1,2,3 trione 1 phenylhydrazine	33
α -Hydroxy- α -methyl- γ -oxoglutaric acid lactone	—	α -Hydroxy- α -methyl- β,γ -dioxoglutaric acid lactone β -phenylhydrazine	181
Ethyl 3-hydroxy-2,5-dioxo-3-cyclopentene-1-carboxylic acid	—	Ethyl 3-hydroxy-2,5 dioxo-4 phenylazo-3-cyclopentene-1-carboxylic acid	182
2,4-Dinitrophenylacetone	—	1-(2,4-Dinitrophenyl)propane-1,2-dione 1-phenylhydrazine	29
2-Nitro-4-carbomethoxyphenylacetone	—	1-(2-Nitro-4-carbomethoxyphenyl)propane-1,2-dione 1-phenylhydrazine	183

Note: References 177-480 are on pp. 130-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

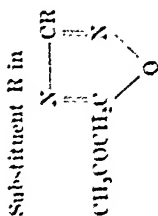
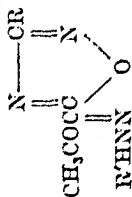
† The formula of the formyl radical is $C_6H_5NHN=CN=NC_6H_5$.

‡ Succinic acid was eliminated.

TABLE I—Continued

A. Monoketones—Continued

Substituents in Product,



Substituent(s) in Aniline	R'	R	Yield, o/a	References
—	Phenyl	Phenyl	40	31, 32
—	Phenyl	<i>p</i> -Tolyl	35	31, 32
2-Methyl	<i>o</i> -Tolyl	<i>p</i> -Tolyl	55	31, 32
4-Methyl	<i>p</i> -Tolyl	<i>p</i> -Tolyl	40	31, 32
2,4-Dimethyl	2,4-Dimethylphenyl	<i>p</i> -Tolyl	40	31, 32
2,5-Dimethyl	2,5-Dimethylphenyl	<i>p</i> -Tolyl	—	32
2-Methoxy	<i>o</i> -Anisyl	<i>p</i> -Tolyl	35	31, 32
3-Methoxy	<i>m</i> -Anisyl	<i>p</i> -Tolyl	35	31, 32
3-Chloro	<i>m</i> -Chlorophenyl	<i>p</i> -Tolyl	55	31, 32
4-Chloro	<i>p</i> -Chlorophenyl	<i>p</i> -Tolyl	30	31, 32
2-Nitro	<i>o</i> -Nitrophenyl	<i>p</i> -Tolyl	45	31, 32
3-Nitro	<i>m</i> -Nitrophenyl	<i>p</i> -Tolyl	20	31, 32
4-Nitro	<i>p</i> -Nitrophenyl	<i>p</i> -Tolyl	20	31, 32
4-Dimethylamino	<i>p</i> -Dimethylaminophenyl	<i>p</i> -Tolyl	25	31, 32
2-Carboxy	<i>o</i> -Carboxyphenyl	<i>p</i> -Tolyl	50	31, 32
4-Carboxy	<i>p</i> -Carboxyphenyl	<i>p</i> -Tolyl	45	31, 32
α -Naphthylamine	α -Naphthyl	<i>p</i> -Tolyl	40	31, 32
<i>p</i> -Naphthylamine	<i>p</i> -Naphthyl	<i>p</i> -Tolyl	35	31, 32
4-Phenyl	<i>p</i> -Biphenyl	<i>p</i> -Tolyl	40	31, 32
4-Benzyl	<i>p</i> -Benzylphenyl	<i>p</i> -Tolyl	45	31, 32
3,3-Dimethoxybenzidine	3,3-Dimethoxybiphenylene	<i>p</i> -Tolyl	20	32
—	Phenyl	<i>p</i> -Tolyl	80	31, 32
2-Methoxy	<i>o</i> -Anisyl	<i>m</i> -Nitrophenyl	50	31, 32

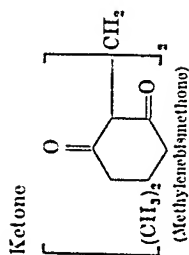
Ketone	Substituent(s) in Aniline	Product (Yield, %)	References
Acetonylpyridinium bromide	—	$\text{CH}_3\text{COC}(\text{NCC}_6\text{H}_5)=\text{NNCC}_6\text{H}_5$ (84)	90
Phenacyl chloride	—	$\text{C}_6\text{H}_5\text{COC}(\text{Cl})=\text{NNHC}_6\text{H}_5$	177
4-Carbomethoxy-3-methyl-5-phenyl-3-cyclohexenone	—	4-Carbomethoxy-3-methyl-5-phenyl-3-cyclohexene-1,2-dione 2-phenylhydrazine	276
4-Carbomethoxy-3-methyl-5-phenyl-3-cyclohexenone	—	4-Carbomethoxy-3-methyl-5-phenyl-3-cyclohexene-1,2-dione 2-phenylhydrazine	276
4-Carbomethoxy-3,5-diphenyl-1,3-cyclohexadien-1-ol	—	4 Carbomethoxy-3,5-diphenyl-3-cyclohexene-1, 2-dione 2-phenylhydrazine	277
Phenyl 2,4-dinitrobenzyl ketone	—	$2,4-(\text{NO}_2)_2\text{C}_6\text{H}_3\text{COC}(\text{C}_6\text{H}_5)=\text{NNHC}_6\text{H}_5$ (quant.)	78
Phenacylpyridinium bromide	—	$\text{C}_6\text{H}_5\text{COC}(\text{NCC}_6\text{H}_5)=\text{NNCC}_6\text{H}_5$ (89)	90
	2-Nitro	$\text{C}_6\text{H}_5\text{COC}(\text{NCC}_6\text{H}_5)=\text{NNCC}_6\text{H}_4\text{NO}_2\text{-o}$	90
	3-Nitro	$\text{C}_6\text{H}_5\text{COC}(\text{NCC}_6\text{H}_5)=\text{NNCC}_6\text{H}_4\text{NO}_2\text{-m}$	90
	4-Nitro	$\text{C}_6\text{H}_5\text{COC}(\text{NCC}_6\text{H}_5)=\text{NNCC}_6\text{H}_4\text{NO}_2\text{-p}$	90
p-Bromophenacylpyridinium bromide	—	$p\text{-BrC}_6\text{H}_4\text{COC}(\text{NCC}_6\text{H}_5)=\text{NNCC}_6\text{H}_5$ (74)	184
5-p-Nitrophenacyl-3-p-tolyl-1,2,4-oxadiazole	—	1-(3-p-Tolyl-1,2,4-oxadiazol-5-yl)-3-p-nitrophenylethane-1,2-dione 1-phenylhydrazine (65)	32
	2-Methoxy	1-(3-p-Tolyl-1,2,4-oxadiazol-5-yl)-3-p-nitrophenylethane-1,2-dione 1-o-methoxyphenylhydrazine (20)	32
	4-Nitro	1-(3-p-Tolyl-1,2,4-oxadiazol-5-yl)-3-p-nitrophenylethane-1,2-dione 1-p-nitrophenylhydrazine (20)	32
Tropinone	—	2,4-Dioxotropinone diphenylhydrazine (80)	34
1-Ethoxalylindene	—	1-Phenylazo-1-ethoxalylindene	35
	3-Nitro	1-m-Nitrophenylazo-1-ethoxalylindene	35
	4-Nitro	1-p-Nitrophenylazo-1-ethoxalylindene	35

Note: References 177-480 are on pp. 136-142.

TABLE I—Continued

A. Monoketones—Continued

Substituent(s) in Aniline	Product (Yield, %)	References
—	2,2'-Methylenebis-(3-hydroxy-5,5-dimethyl-6-phenylazo-2-cyclohexen-1-one) (quant.)	186, 185
2-Methyl	2,2'-Methylenebis-(3-hydroxy-5,5-dimethyl-6-oxo-2-cyclohexen-1-one)	185, 186
2,3-Dimethyl	2,2'-Methylenebis-[3-hydroxy-5,5-dimethyl-6-(2,3-xylylazo)-2-cyclohexen-1-one]	185, 186
2,5-Dimethyl	2,2'-Methylenebis-(3-hydroxy-5,5-dimethyl-6-oxo-2-cyclohexen-1-one)	185
4-Bromo	2,2'-Methylenebis-(3-hydroxy-5,5-dimethyl-6-oxo-2-cyclohexen-1-one)	185, 186
α -Naphthylamine	2,2'-Methylenebis-(3-hydroxy-5,5-dimethyl-6-oxo-2-cyclohexen-1-one)	185, 186
β -Naphthylamine	2,2'-Methylenebis-(3-hydroxy-5,5-dimethyl-6-oxo-2-cyclohexen-1-one)	185, 186
Benzidine	?	185, 186
4-Bromo	N,N'-Di-(<i>p</i> -bromophenyl)-C-2-quinolylformazan (79)	186
4-Bromo	N,N'-Di-(<i>p</i> -bromophenyl)-C-2-quinolylformazan (78)	36a
4-Bromo	N,N'-Di-(<i>p</i> -bromophenyl)-C-2-quinazolylformazan	36a
4-Bromo	N,N'-Di-(<i>p</i> -bromophenyl)-C-2-quinazolylformazan (76)	36a
4-Bromo	N,N'-Di-(<i>p</i> -bromophenyl)-C-2-benzoxazolylformazan	36a



Ethyl 2-quinolylpyruvate
 Ethyl 2-quinolylpyruvate
 Ethyl 2-quinazolylpyruvate
 Ethyl 2-benzoxazolylpyruvate

Ethyl 2 benzothiazolylpyruvate	4-Bromo	N,N'-Di-(<i>p</i> -bromophenyl)-C-(2-benzothiazolyl)formazan (32)	36a
Ethyl 2-oxo-5-(2-benzoxazolyl)-4-pentenoate	4-Bromo	N,N'-Di-(<i>p</i> -bromophenyl)-C-(2-(2-benzoxazolyl)vinyl)formazan	36a
Ethyl 2-oxo-5-(2-benzothiazolyl)-4-pentenoate	4-Bromo	N,N'-Di-(<i>p</i> -bromophenyl)-C-(2-(2-benzothiazolyl)vinyl)formazan (46)	36a

B. β -Ketoaldehydes			References
Substituent(s) in Aniline	Product (Yield, %)		
—	$\text{CH}_3\text{COC}(\text{CHO})=\text{NNHC}_6\text{H}_5$		49
4-Nitro	$\text{CH}_3\text{COC}(\text{CHO})=\text{NNHC}_6\text{H}_4\text{NO}_2$ - <i>p</i> (17)		19c
—	$\text{C}_2\text{H}_5\text{COC}(\text{CHO})=\text{NNHC}_6\text{H}_5$		50
—	$(\text{CH}_3)_2\text{C}=\text{CHCOC}(\text{CHO})=\text{NNHC}_6\text{H}_5$		51
—	$\text{C}_6\text{H}_5\text{COC}(\text{CHO})=\text{NNHC}_6\text{H}_5$		49
—	<i>p</i> - $\text{CH}_3\text{C}_6\text{H}_4\text{COC}(\text{CHO})=\text{NNHC}_6\text{H}_5$		50*
—	<i>p</i> - $\text{CH}_3\text{OC}_6\text{H}_4\text{COC}(\text{CHO})=\text{NNHC}_6\text{H}_5$		50

C. β -Diketones

Substituent(s) in Aniline*	Product (Yield, %)	References
—	$\text{CH}_3\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_5$	12, 187, 188
4-Methyl	$\text{CH}_3\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4\text{CH}_3$ - <i>p</i> (92)	189
4-Bromo	$\text{CH}_3\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4\text{Br}$ - <i>p</i>	190
2,4-Dibromo	$\text{CH}_3\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_3\text{Br}_2$ -2,4	190
2,4,6-Tribromo	$\text{CH}_3\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_2\text{Br}_3$ -2,4,6	190
2-Nitro	$\text{CH}_3\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2$ - <i>o</i>	188, 190

Note: References 177-480 are on pp. 136-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

§ These compounds are named as derivatives of the hypothetical formazan, $\text{H}_2\text{NN}=\text{CHN}=\text{NH}$.

TABLE I—Continued
C. *β*-Diketones—Continued

<i>β</i> -Diketone	Substituent(s) in Aniline*	Product (Yield, %)	References
Pentane-2,4-dione (Cont.)	3-Nitro	$\text{CH}_3\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2$ - <i>m</i>	188
	4-Nitro	$\text{CH}_3\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2$ - <i>p</i>	188, 190
	4-Methyl-3-nitro	$\text{CH}_3\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_3(\text{CH}_3)-4\text{-NO}_2$ -3	189
	4-Bromo-2-nitro	$\text{CH}_3\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_3(\text{Br})-4\text{-NO}_2$ -2	190
	2,4-Dibromo-6-nitro	$\text{CH}_3\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_2(\text{Br})_2-2,4\text{-NO}_2$ -6	190
	Benidine	3,3'-(4,4'-Biphenylene)dihydrazono)bis(pentane-2,3,4-trione)	191, 192
	3,3'-Dimethylbenzidine	3,3'-(3,3'-Dimethyl-4,4'-biphenylene)dihydrazono)bis(pentane-2,3,4-trione)	191, 192
	3,3'-Dimethoxybenzidine	3,3'-(3,3'-Dimethoxy-4,4'-biphenylene)dihydrazono)bis(pentane-2,3,4-trione)	191, 192
	4-(3-Methyl-5-phenylpyrazol-1-yl)	Pentane-2,3,4-trione 3-arylhydrazono	193
	1-Phenyl-2,3-dimethyl-4-amino-5-isopyrazolone	Pentane-2,3,4-trione 3-arylhydrazono	194
	1-Phenyl-3,5-dimethyl-4-aminopyrazole	Pentane-2,3,4-trione 3-arylhydrazono	195
	3,5-Dimethyl-4-aminopyrazole	Pentane-2,3,4-trione 3-arylhydrazono	196
	5-Amino-3-isopropyl-1,2,4-triazole	Pentane-2,3,4-trione 3-arylhydrazono	197
Pentane-2,4-dione enol ethyl ether	4-Nitro	$\text{CH}_3\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2$ - <i>p</i>	198
1,5-Dichloropentane-2,4-dione	4-Nitro	$\text{ClCH}_2\text{COC}(\text{COCH}_2\text{Cl})=\text{NNHC}_6\text{H}_4\text{NO}_2$ - <i>p</i>	199
Hexane-2,4-dione	4-Nitro	$\text{CH}_3\text{COC}(\text{COC}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{NO}_2$ - <i>p</i>	199
Heptane-2,4-dione	—	$\text{CH}_3\text{COC}(\text{COCH}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_5$	200

6-Methyl heptane-2,4-dione	4-Nitro	$(\text{CH}_3)_2\text{CHCH}_2\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	199
Heptane-3,5-dione	4-Chloro	$\text{C}_6\text{H}_5\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4\text{Cl-}p$	199
Heptane-2,4,6-trione	—	$(\text{C}_6\text{H}_5)_2\text{NHN}=\text{CHCOCHN}=\text{NC}_6\text{H}_5)_2\text{CO}$	201
Nonane-1,6-dione	—	2,6-Dimethyl-3,5-diphenylazopyrone	202
1-Phenylbutane-1,3-dione	4-Chloro	$n\text{-C}_6\text{H}_5\text{COC}(\text{COCH}_3)_2=\text{NNHC}_6\text{H}_4\text{Cl-}p$	199
	4-Nitro	$n\text{-C}_6\text{H}_5\text{COC}(\text{COCH}_3)_2=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	199
	—	$\text{C}_6\text{H}_5\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_5$ (90)	42, 187
	—	$\text{C}_4\text{H}_9\text{N}=\text{NC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_5$ (25)	203, 204
	2-Nitro	$\text{C}_6\text{H}_5\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}o$	205
	4-Nitro	$\text{C}_6\text{H}_5\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$ (quant.)	205, 206
4-Acetamido	4-Nitro	$\text{C}_6\text{H}_5\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4\text{NHCOCCH}_3\text{-}p$	207
2,4-Dibromo	2,4-Dibromo	$\text{C}_6\text{H}_5\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_2\text{Br}_2\text{-}2,4$	42
2,4,6-Tribromo	2,4,6-Tribromo	$\text{C}_6\text{H}_5\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_2\text{Br}_3\text{-}2,4,6$	42
3,5-Dimethyl-4-aminopyrazole	3,5-Dimethyl-4-aminopyrazole	1-Phenylbutane-1,2,3-trione 2-(3,5-dimethyl-4-pyrazolyl)hydrazine	196
1-o-Anisylbutane-1,3-dione	4-Nitro	$o\text{-CH}_3\text{OC}_6\text{H}_4\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	203
1-(2,4-Dimethoxyphenyl)butane-1,3-dione	4-Nitro	2,4-(CH_3O) $_2\text{C}_6\text{H}_3\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	203
1-(2,4-Diethoxyphenyl)butane-1,3-dione	—	2,4-($\text{C}_2\text{H}_5\text{O}$) $_2\text{C}_6\text{H}_3\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4$ (good)	210, 209
1-Phenylpentane-2,4-dione	4-Nitro	$\text{C}_6\text{H}_5\text{CH}_2\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	199
2,6-Dimethylnonane-4,6-dione	4-Nitro	$[(\text{CH}_3)_2\text{CHCH}_2\text{CO}]_2\text{C}=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	199
1-Phenylhexane-3,5-dione	4-Nitro	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{COC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$ (70)	211
1,3-Diphenylpropane-1,3-dione	—	$(\text{C}_6\text{H}_5)_2\text{C}=\text{NNHC}_6\text{H}_5$	187
	4-Nitro	$(\text{C}_6\text{H}_5)_2\text{C}=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	199
	4-Sulfo	$(\text{C}_6\text{H}_5)_2\text{C}=\text{NNHC}_6\text{H}_4\text{SO}_3\text{H-}p$	187
1,3-Di-p-nitrophenylpropane-1,3-dione	4-Nitro	$(p\text{-O}_2\text{NC}_6\text{H}_4\text{CO})_2\text{C}=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	199

Note: References 177-480 are on pp. 136-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.
 † This product was obtained by the use of excess diazonium salt.

TABLE I—Continued
C. β -Diketones—Continued

Substituent(s) in Aniline*	Product (Yield, %)	References
β -Diketone		
1-(3,5-Dimethoxyphenyl)-3-phenylpropane-1,3-dione	3,5-(CH ₃ O) ₂ C ₆ H ₃ COC(COC ₆ H ₅) ₂ =NNHC ₆ H ₅	212
1-(2,4,6-Trimethoxyphenyl)-3-phenylpropane-1,3-dione	2,4,6-(CH ₃ O) ₃ C ₆ H ₂ COC(COC ₆ H ₅) ₂ =NNHC ₆ H ₅	209
1-(2,4,6-Trimethoxyphenyl)-3- <i>p</i> -anisylpropane-1,3-dione	2,4,6-(CH ₃ O) ₃ C ₆ H ₂ COC(COC ₆ H ₄ OCH ₃ - <i>p</i>)=NNHC ₆ H ₅	209
1-(2,4,6-Trimethoxyphenyl)-3-(2-ethoxyphenyl)propane-1,3-dione	2,4,6-(CH ₃ O) ₃ C ₆ H ₂ COC(COC ₆ H ₄ OC ₂ H ₅ - <i>p</i>)=NNHC ₆ H ₅	209
1-(2,4,6-Trimethoxyphenyl)-3-(3-methoxy-4-ethoxyphenyl)propane-1,3-dione	2,4,6-(CH ₃ O) ₃ C ₆ H ₂ COC(COC ₆ H ₃ OCH ₃ -3-OC ₂ H ₅ -4)=NNHC ₆ H ₅	209
1,4-Diphenylbutane-1,3-dione	C ₆ H ₅ CH ₂ COC(COC ₆ H ₅) ₂ =NNHC ₆ H ₅ (quant.)	213
1,5-Diphenylpentane-2,4-dione	(C ₆ H ₅ CH ₂ CO) ₂ C=NNHC ₆ H ₄ NO ₂ - <i>p</i>	199
1-(2-Hydroxy-1-naphthyl)-3-phenylpropane-1,2,3-trione	1-(2-Hydroxy-1-naphthyl)-3-phenylpropane-1,2,3-trione 2-phenylhydrazone (79)	214
α,γ -Dioxovaleric acid	CH ₃ COC(COCO ₂ H)=NNHC ₆ H ₅	215
Ethyl α,γ -dioxovulgate	CH ₃ COC(COCO ₂ C ₂ H ₅)=NNHC ₆ H ₅	216, 187
	CH ₃ COC(COCO ₂ C ₂ H ₅)=NNHC ₆ H ₄ CH ₃ - <i>o</i> (78)	216
	CH ₃ COC(COCO ₂ C ₂ H ₅)=NNHC ₆ H ₄ CH ₃ - <i>p</i> (98)	216
	CH ₃ COC(COCO ₂ C ₂ H ₅)=NNHC ₆ H ₄ Cl- <i>m</i> (99)	216
	CH ₃ COC(COCO ₂ C ₂ H ₅)=NNHC ₆ H ₄ Br- <i>m</i> (99)	216
	CH ₃ COC(COCO ₂ C ₂ H ₅)=NNHC ₆ H ₄ NO ₂ - <i>o</i> (73)	216
	CH ₃ COC(COCO ₂ C ₂ H ₅)=NNHC ₆ H ₄ NO ₂ - <i>m</i> (90)	216
	CH ₃ COC(COCO ₂ C ₂ H ₅)=NNHC ₆ H ₄ NO ₂ - <i>p</i> (76)	216

Diethyl xanthochelidonate	—	Diethyl β,δ diphenylazoxanthochelidonate [¶]	202
α,γ -Dioxo- γ -phenylbutyric acid	—	$C_6H_5COC(COCO_2H)=NNHC_6H_5$	217
Ethyl α,γ -dioxo- γ -phenylbutyrate	—	$C_6H_5COC(COCO_2C_2H_5)=NNHC_6H_5$	187, 217
2 Carboxy Benzidine	—	$C_6H_5COC(COCO_2C_2H_5)=NNHC_6H_4CO_2H$	217
—	—	$\beta,\beta'-(4,4'-\text{Diphenylene})\text{dihydrazono}[\text{bis}(\text{ethyl } \alpha,\beta,\gamma\text{-trioxo-}\gamma\text{-phenylbutyrate})]$	217
Ethyl α,γ -dioxo- γ -(<i>p</i> -acetamidophenyl)butyrate	—	Ethyl α,β,γ -trioxo- γ -(<i>p</i> -acetamidophenyl)butyrate	218
Ethyl 2,4-dioxo- δ -methyl-5-heptenoate	4-Nitro	β -phenylhydrazone	—
Ethyl α,γ -dioxo- γ [<i>p</i> -(3,4-dicarbethoxy-2,5-dimethyl-pyrazol-1-yl)phenyl]butyrate	—	Ethyl 1,2,3,4-trioxo- δ -methyl-5-heptenoate	0
—	—	3- <i>p</i> -nitrophenylhydrazone	—
—	—	Ethyl α,β,γ -trioxo- γ [<i>p</i> -(3,1-dicarbethoxy-2,5-dimethylpyrazol-1-yl)phenyl]butyrate	219
—	—	β -phenylhydrazone	—
Cyclohexane-1,3-dione	4-Methyl	<i>D</i> Cyclic β -Diketones	43
5,5-Dimethylcyclohexane-1,3-dione (methone)	—	Cyclohexane-1,2,3-trione 2- <i>p</i> -tolylhydrazone	44, 45
—	—	5,5-Dimethylcyclohexane-1,2,3-trione 2-phenylhydrazone	—
2-Methyl	2-Methyl	5,5-Dimethylcyclohexane-1,2,3-trione 2- <i>o</i> -tolylhydrazone	45
3-Methyl	3-Methyl	5,5-Dimethylcyclohexane-1,2,3-trione 2- <i>m</i> -tolylhydrazone	45
4-Methyl	4-Methyl	5,5-Dimethylcyclohexane-1,2,3-trione 2- <i>p</i> -tolylhydrazone	45
4-Nitro	4-Nitro	5,5-Dimethylcyclohexane-1,2,3-trione 2- <i>p</i> -nitrophenylhydrazone	46

Note: References 177-480 are on pp. 136-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.
 ¶ Other products were also isolated from the reaction mixture.

TABLE I—Continued
D. Cyclic β -Diketones—Continued

β -Diketone	Substituent(s) in Aniline*	Product (Yield, %)	References
5,5-Dimethylcyclohexane-1,3-dione (methone) (Cont.)			
	2-Arsono	5,5-Dimethylcyclohexane-1,2,3-trione 2- <i>o</i> -arsonophenylhydrazine	220
	3-Arsono	5,5-Dimethylcyclohexane-1,2,3-trione 2- <i>m</i> -arsonophenylhydrazine	220
	4-Arsono	5,5-Dimethylcyclohexane-1,2,3-trione 2- <i>p</i> -arsonophenylhydrazine	220
	α -Naphthylamine	5,5-Dimethylcyclohexane-1,2,3-trione 2- α -naphthylhydrazine	45
	β -Naphthylamine	5,5-Dimethylcyclohexane-1,2,3-trione 2- β -naphthylhydrazine	45
	Benzidine	2,2'-(4,4'-Biphenylenedihydrazono)bis-[5,5-dimethylcyclohexane-1,2,3-trione]	46
	3,3'-Dimethylbenzidine	2,2'-(3,3'-Dimethyl-4,4'-biphenylenedihydrazono)bis-[5,5-dimethylcyclohexane-1,2,3-trione]	46
	3,3'-Dimethoxybenzidine	2,2'-(3,3'-Dimethoxy-4,4'-biphenylenedihydrazono)bis-[5,5-dimethylcyclohexane-1,2,3-trione]	46
5-Phenylcyclohexane-1,3-dione	—	5-Phenylcyclohexane-1,2,3-trione 2-phenylhydrazine (quant.)	221

4-Cyano 5-phenylcyclohexane-1,3-dione	—	4-Cyano-5-phenylcyclohexane-1,2,3-trione 2-phenylhydrazono	43
4 Carbethoxy 5 phenylcyclohexane-1,3 dione	—	4-Carbethoxy-5 phenylcyclohexane-1,2,3-trione 2-phenylhydrazono	43
5 (2-Furyl)cyclohexane-1,3-dione	—	5-(2-Furyl)cyclohexane-1,2,3-trione 2-phenylhydrazono	221
Phthalic acid	—	0,0-Dimethylcyclohexane 1,2,3,4,5-pentaone 2,4-diphenylhydrazono	222
2-Butyryl-6,6 dimethylcyclohexane-1,3,5 trione	—	2-Butyryl 0,0-dimethylcyclohexane-1,3,4,5-tetraone 4-phenylhydrazono	222
2,2'-Methylenebis-(0,6 dimethylcyclohexane-1,3,5-tione)	—	2,2'-Methylenebis-(0,6-dimethylcyclohexane-1,3,4,5-tetraone 4-phenylhydrazono)	223
Indan-1,3 dione	—	Indan-1,2,3-trione 2-phenylhydrazono (35)	47
4-Methyl	4-Methyl	Indan-1,2,3-trione 2- <i>p</i> -tolylhydrazono	48
4-Nitro	4-Nitro	Indan 1,2,3 tione 2- <i>p</i> -nitrophenylhydrazono	48
β -Naphthylamine	β -Naphthylamine	Indan-1,2,3 tione 2- β naphthylhydrazono	48
Benzidine	Benzidine	2,2'-(4,4'-Biphenylene)dihydrazono)bis(indan-1,2,3-trione)	18
2,4-Dioxo-1,2,3,4,1 α ,9,10,10 α -octahydrophenanthrene	—	2,3,4-Trioxo-1,2,3,4,1 α ,9,10,10 α -octahydrophenanthrene 3 phenylhydrazono	224

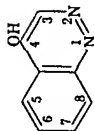
Note: References 177-480 are on pp. 136-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

TABLE I—Continued

E. 4-Hydroxycinnolines from o-Aminoketones

Substituent(s) in 4-Hydroxycinnoline
(Yield, %)



Reactant	References
<i>Acetophenone</i>	
2-Amino	37, 22, 39
2-Amino-4-methyl	164
2-Amino-3-methyl	164
2-Amino-6-methoxy	224a
2-Amino-5-methoxy	224a
2-Amino-4-methoxy	224a
2-Amino-3-methoxy	167a
2-Amino-5-chloro	22, 39
2-Amino-4-chloro	37, 39, 161
2-Amino-3-chloro	22
2-Amino-5-bromo	39, 22
2-Amino-3-bromo	22
2-Amino-5-iodo	39
2-Amino-6-nitro	165
2-Amino-5-nitro	39, 22, 159
2-Amino-4-nitro	165, 166
2-Amino-3-nitro	163, 164
	164
2-Amino-5-cyano	22
2-Amino-4-acetyl	165
2-Amino-5-acetamido	39
2-Amino-phenylazo	166
2-Amino-5-(3-acetylphenylazo)	166
— (70-75)	
7-Methyl (58)	
8-Methyl (78)	
5-Methoxy (55)	
6-Methoxy (53)	
7-Methoxy (63)	
8-Methoxy (92)	
6-Chloro (74)	
7-Chloro (90-95)	
8-Chloro (69)	
6-Bromo (95)	
8-Bromo (57)	
6-Iodo	
5-Nitro (70)	
6-Nitro (87)	
7-Nitro (76)	
8-Nitro (70)	
8-Chloro** (45)	
6-Cyano (70-90)	
7-Acetyl (47)	
6-Acetamido (33)	
6-Phenylazo (60)	
6-(3-Acetylphenylazo) (50)	

2-Amino-4,5-dimethyl	38	6,7-Dimethyl (91)	38
2-Amino-4,5-dimethoxy	107b	6,7-Dimethoxy (67)	107b
2-Amino-4,5-dichloro	162	6,7-Dichloro (91)	162
2-Amino-3,4-dichloro	162	7,8-Dichloro (59)	162
2-Amino-3,5-dibromo	39	6,8-Dibromo (65)	39
2-Amino-5-chloro-1-methyl	102, 24	6-Chloro-7-methyl (90)	102, 24
2-Amino-3-chloro-4-methyl	162	8-Chloro-7-methyl (75)	162
2-Amino-5-bromo-4-methyl	102	6-Bromo-7-methyl (37)	102
2-Amino-4-methyl-5-nitro	104	7-Methyl-6-nitro (76)	104
2-Amino-4-chloro-5-nitro	101	7-Chloro-6-nitro (57)	101
2-Amino-1-chloro-3-nitro	161	7-Chloro-8-nitro (57)	161
<i>Phenacyl Chloride</i>			
2-Amino	24	3-Chloro (55)	24
2-Amino-5-methyl	38	3-Chloro-6-methyl (87)	38
2-Amino-5-chloro	24	3,6-Dichloro (73)	24
2-Amino-4,5-dimethyl	38	3 Chloro 6,7-dimethyl (80)	38
<i>Phenacyl Bromide</i>			
2-Amino	24	3-Bromo (73)	24
2-Amino-5-chloro	24	3-Bromo-6-chloro (77)	24
2-Amino-5-bromo	24	3,6-Dibromo (76)	24
<i>Propiophenone</i>			
2-Amino	40, 39	3-Methyl (83)	40, 39
2-Amino-5-chloro	40	6-Chloro-3-methyl (94)	40
2-Amino-5-bromo	39, 40	6-Bromo-3-methyl (76)	39, 40
2-Amino-5-nitro	39, 40	3-Methyl-6-nitro (65)	39, 40
2-Amino-3-nitro	40	3-Methyl-8-nitro (96)	40

Note: Its forewax 177-180 are on pp. 136-142.

** The 8-chloro compound is obtained if the diazotization is run in hydrochloric acid.

TABLE I—Continued
E. 4-Hydroxycinnolines from o-aminoketones—Continued

Reactant	Substituent in 4-Hydroxycinnoline (Yield, %)	References
<i>Miscellaneous o-aminoketones</i>		
2-Aminobutyrophenone	3-Ethyl (68)	41
γ -(2-Aminobenzoyl)butyric acid	3-Carboxyethyl (53)	41
β -(2-Amino-4,5-dimethoxybenzoyl)propionic acid	3-Carboxymethyl-6,7-dimethoxy (71)	22
Ethyl β -(2-amino-4-carbethoxybenzoyl)propionate	3-Carbethoxymethyl-7-carbethoxy (13)	160
3,3'-Diacetyl-4,4'-diaminoazobenzene	4,4'-Dihydroxy-6,6'-azocinnoline (69)	166
5-Amino-6-acetyllindane	6,7-Cyclopenteno (60)	38
4-Amino-5-acetyllindane	7,8-Cyclopenteno	38
5-Amino-6-chloroacetyllindane	3-Chloro-6,7-cyclopenteno (57)	38
1,2,3,4-Tetrahydro-6-amino-7-acetylnaphthalene	6,7-Cyclohexeno (70)	38
1,2,3,4-Tetrahydro-5-amino-6-acetylnaphthalene	7,8-Cyclohexeno	38
1,2,3,4-Tetrahydro-6-amino-7-chloroacetylnaphthalene	3-Chloro-6,7-cyclohexeno (67)	38

Note: References 177-180 are on pp. 130-142.

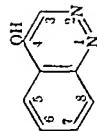


TABLE II

COUPLING OF DIAZONIUM SALTS WITH β -KETO ACIDS, ESTERS, AND AMIDES

A. β -Keto Acids		References
Substituent(s) in Aniline*	Product (Yield, %)	
—	$\text{CH}_3\text{COCH}=\text{NNHC}_6\text{H}_5$ (73-82)	55, 53, 54, 225
4-Methyl	$\text{CH}_3\text{COC}(\text{N}=\text{NC}_6\text{H}_5)=\text{NNHC}_6\text{H}_5$ † (41)	52, 226
2-Methoxy	$\text{C}_6\text{H}_5\text{C}(\text{N}=\text{NC}_6\text{H}_5)=\text{NNHC}_6\text{H}_5$ ‡	140
2-Nitro	$\text{CH}_3\text{COC}(\text{N}=\text{NC}_6\text{H}_4\text{CH}_3\text{-}p)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-}p$ †	52
3-Nitro	$\text{CH}_3\text{COCH}=\text{NNHC}_6\text{H}_4\text{OCH}_3\text{-}o$	227
4-Nitro	$\text{CH}_3\text{COCH}=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}o$	228, 229
2,4-Dibromo	$\text{CH}_3\text{COCH}=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}m$	228
2-Bromo-4-nitro	$\text{CH}_3\text{COCH}=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	228
2,4,6-Trichloro	$\text{CH}_3\text{COCH}=\text{NNHC}_6\text{H}_3\text{Br}_2\text{-}2,4$	152
2,4,6-Tribromo	$\text{CH}_3\text{COCH}=\text{NNHC}_6\text{H}_3\text{Br-}2\text{-NO}_2\text{-}4$	228
2,6-Dibromo-4-nitro	$\text{CH}_3\text{COCH}=\text{NNHC}_6\text{H}_3\text{Cl}_2\text{-}2,4,6$	230
α -Naphthylamine	$\text{CH}_3\text{COCH}=\text{NNHC}_6\text{H}_2\text{Br}_2\text{-}2,6\text{-NO}_2\text{-}4$	230
4-Nitro	$\text{CH}_3\text{COCH}=\text{NNHC}_{10}\text{H}_7\text{-}\alpha$	228
—	$\text{CH}_3\text{COC}(\text{N}=\text{NC}_6\text{H}_4\text{-}\alpha)=\text{NNHC}_{10}\text{H}_7\text{-}\alpha$ †	225
—	$\text{C}_6\text{H}_5\text{COCH}=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	52
—	$\text{C}_6\text{H}_5\text{C}(\text{N}=\text{NC}_6\text{H}_5)=\text{NNHC}_6\text{H}_5$ †	130a
—	γ -Hydroxy- α,β -dioxobutyric acid lactone β -phenylhydrazide	153
—	$\text{C}_6\text{H}_5\text{COCH}=\text{NNHC}_6\text{H}_5$	231
—	$\text{C}_6\text{H}_5\text{COC}(\text{N}=\text{NC}_6\text{H}_5)=\text{NNHC}_6\text{H}_5$ † (39)	232
		204, 203

Note: References 177-180 are on pp. 130-142.

* The full name is given when it is awkward to name the aryl amino as a derivative of aniline.

† This product was obtained when 2 equivalents of the diazonium salt were used.

‡ This product was obtained when 3 equivalents of the diazonium salt were used.

TABLE II—Continued

1. β -Keto Acids—Continued		
β -Keto Acid	Substituent(s) in Aniline*	Product (Yield, %)
Benzoylacetate acid (Cont.)	1-Methoxy	$C_6H_5COCH=NSHC_6H_4OCH_3$ ^p
	1-Chloro	$C_6H_5COCH=NSHC_6H_4Cl$ ^p
	2-Nitro	$C_6H_5COCH=NSHC_6H_4NO_2$ ^o
	3-Nitro	$C_6H_5COCH=NSHC_6H_4NO_2$ ^o
	4-Nitro	$C_6H_5COCH=NSHC_6H_4NO_2$ ^p
	4-Carboxy	$C_6H_5COCH=NSHC_6H_4CO_2H$ ^p
o-Carboxybenzoylacetate acid Acetonedicarboxylic acid	2-Hydroxy-5-chloro	$o-HO-C_6H_4COCH=NSHC_6H_4OH-2,4,5$ $COCH=NSHC_6H_4$ ^o (39)
	—	$COCH=NSHC_6H_4CH_3$ ^o (50)
	4-Methyl	$COCH=NSHC_6H_4CH_3$ ^o (50)
2-Oxo-1-propanesulfonic acid	1-Chloro	$CH_3COC(SO_3H)=NSHC_6H_4$
	—	$CH_3COC(SO_3H)=NSHC_6H_4Cl$ ^p
	1-Chloro	$CH_3COC(SO_3H)=NSHC_6H_4Cl$ ^p
	1-Bromo	$CH_3COC(SO_3H)=NSHC_6H_4Br$ ^p
	2-Nitro	$CH_3COC(SO_3H)=NSHC_6H_4NO_2$ ^o
	3-Nitro	$CH_3COC(SO_3H)=NSHC_6H_4NO_2$ ^o
	4-Nitro	$CH_3COC(SO_3H)=NSHC_6H_4NO_2$ ^p
	2,4-Dichloro	$CH_3COC(SO_3H)=NSHC_6H_3Cl_2$ ^{2,4}
	2,4-Dibromo	$CH_3COC(SO_3H)=NSHC_6H_3Br_2$ ^{2,4}
2-Oxo-2-phenyl-1-ethane- sulfonic acid	—	$C_6H_5COC(SO_3H)=NSHC_6H_5$ ^{2,4}
	1-Chloro	$C_6H_5COC(SO_3H)=NSHC_6H_4Cl$ ^{2,4}
	1-Bromo	$C_6H_5COC(SO_3H)=NSHC_6H_4Br$ ^{2,4}
	2-Nitro	$C_6H_5COC(SO_3H)=NSHC_6H_4NO_2$ ^o
	4-Nitro	$C_6H_5COC(SO_3H)=NSHC_6H_4NO_2$ ^p
	2,4-Dichloro	$C_6H_5COC(SO_3H)=NSHC_6H_3Cl_2$ ^{2,4}
	2,4-Dibromo	$C_6H_5COC(SO_3H)=NSHC_6H_3Br_2$ ^{2,4}
	2,4,6-Trichloro	$C_6H_5COC(SO_3H)=NSHC_6H_2Cl_3$ ^{2,4,6}

2-Bromo-6-methyl-4-nitro	Ethyl α,β -dioxobutyrate α -(2-bromo-6-methyl-4-nitrophenylhydrazine)	247
4-Bromo-2-methyl-6-nitro	Ethyl α,β -dioxobutyrate α -(4-bromo-2 methyl-6-nitrophenylhydrazine)	247
2,6-Dibromo-3-nitro-4-methyl	Ethyl α,β -dioxobutyrate α -(2,6-dibromo-3-nitro-4-methylphenylhydrazine)	247
4,6-Dibromo-2-methyl-5-nitro	Ethyl α,β -dioxobutyrate α -(4,6 dibromo-2-methyl-5-nitrophenylhydrazine)	247
α -Naphthylamine	Ethyl α,β -dioxobutyrate α -(α naphthylhydrazine) (quant.)	249, 237
β -Naphthylamine	Ethyl α,β dioxobutyrate α (β -naphthylhydrazine)	237, 249
2-Aminocanthra-quinone	Ethyl α,β -dioxobutyrate α -(2-anthraquinonylhydrazine) (quant.)	250
3-Aminocarbazole	Ethyl α,β -dioxobutyrate α -(3-carbazolyhydrazine)	251
N-Ethyl 3-aminocarbazole	Ethyl α,β -dioxobutyrate α -(N-ethyl-3-carbazolyhydrazine)	251
p-(3-Carboxy-4-hydroxyphenylazo)	Ethyl α,β dioxobutyrate α -arylhydrazine	252
p-(p-Dimethylsulfamylphenylsulfamyl)	Ethyl α,β -dioxobutyrate α -(p-(p-dimethylsulfamylphenylsulfamyl)phenylhydrazine)	244
3,5-Dimethyl-4-aminopyrazole	Ethyl α,β -dioxobutyrate α -(3,5-dimethyl-4-pyrazolyhydrazine)	196
1-Phenyl 3,5-dimethyl-4-aminopyrazole	Ethyl α,β -dioxobutyrate α -(1-phenyl-3,5-dimethyl-4-pyrazolyhydrazine)	195
p-(3,4-Dicarbomethoxy-5-methyl-1-pyrazolyl)	Ethyl α,β -dioxobutyrate α -arylhydrazine	253

Note: References 177-480 are on pp. 130-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

TABLE II—Continued

<i>B. β-Keto Esters—Continued</i>		References
β -Keto Ester	Substituent(s) in Aniline*	
Ethyl acetoacetate (<i>Cont.</i>)	3-Amino-5-isopropyl-1,2,4-triazole	Product (Yield, %)
	Benzidine	Ethyl α,β -dioxobutyrate α -(5-isopropyl-1,2,4-triazol-3-yl-)hydrazine
<i>l</i> -Menthyl acetoacetate	3,3'-Dicarboxybenzidine	α,α' -(4,4'-Biphenylenedihydrazono)bis(ethyl α,β -dioxobutyrate) (98)
	—	α,α' -(3,3'-Dicarboxy-4,4'-biphenylenedihydrazono)bis(ethyl α,β -dioxobutyrate)
Methyl γ -chloroacetoacetate	4-Methyl	$\text{CH}_3\text{COC}(\text{CO}_2\text{C}_{10}\text{H}_{19})=\text{NNHC}_6\text{H}_5$
	4-Chloro	$\text{CH}_3\text{COC}(\text{CO}_2\text{C}_{10}\text{H}_{19})=\text{NNHC}_6\text{H}_4\text{CH}_3$ - <i>p</i>
Ethyl γ -chloroacetoacetate	4-Bromo	<i>p</i> - $\text{CH}_3\text{C}_6\text{H}_4\text{N}=\text{NC}(\text{CO}_2\text{C}_{10}\text{H}_{19})=\text{NNHC}_6\text{H}_4\text{CH}_3$ - <i>p</i> †
	—	$\text{CH}_3\text{COC}(\text{CO}_2\text{C}_{10}\text{H}_{19})=\text{NNHC}_6\text{H}_4\text{Cl}$ - <i>p</i>
Methyl γ -chloroacetoacetate	2-Methyl	$\text{CH}_3\text{COC}(\text{CO}_2\text{C}_{10}\text{H}_{19})=\text{NNHC}_6\text{H}_4\text{Br}$ - <i>p</i>
	4-Methyl	$\text{ClCH}_2\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_5$
Methyl γ -chloroacetoacetate	—	$\text{ClCH}_2\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_4\text{CH}_3$ - <i>o</i>
	2-Methyl	$\text{ClCH}_2\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_4\text{CH}_3$ - <i>p</i>
Ethyl γ -chloroacetoacetate	4-Methyl	$\text{ClCH}_2\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_4\text{CH}_3$ - <i>p</i>
	—	$\text{ClCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_5$
Methyl γ -chloroacetoacetate	2-Methyl	$\text{ClCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3$ - <i>o</i>
	4-Methyl	$\text{ClCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3$ - <i>p</i>
Ethyl γ -chloroacetoacetate	4-Chloro	$\text{ClCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{Cl}$ - <i>p</i>
	4-Nitro	$\text{ClCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{NO}_2$ - <i>p</i>
Methyl γ -chloroacetoacetate	2,4-Dichloro	$\text{ClCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_3\text{Cl}_2$ -2,4
	2,4,6-Trichloro	$\text{ClCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_3\text{Cl}_3$ -2,4,6
Ethyl γ -chloroacetoacetate	2,4,6-Tribromo	$\text{ClCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_2\text{Br}_3$ -2,4,6
	2-Chloro-4-nitro	$\text{ClCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_3\text{Cl}_2\text{NO}_2$ -4
Ethyl γ -chloroacetoacetate	2,6-Dichloro-4-nitro	$\text{ClCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_2\text{Cl}_2\text{NO}_2$ -2,6
	—	$\text{ClCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_2\text{Cl}_2\text{NO}_2$ -2,6

Methyl γ -bromoacetoacetate	—	$n\text{-C}_4\text{H}_9\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_5$	258
Ethyl γ -bromoacetoacetate	—	$\text{BrCH}_2\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_5$	258
	2-Methyl	$\text{BrCH}_2\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_4\text{CH}_3$	258
	4-Methyl	$\text{BrCH}_2\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_4\text{CH}_3$	258
	—	$\text{BrCH}_2\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_4\text{CH}_3$	258
	2-Methyl	$\text{BrCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_5$ (good)	259, 230,
	4-Methyl	$\text{BrCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_5$	258
	4-Bromo	$\text{BrCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3$	258
	2-Nitro	$\text{BrCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{Br}$	258
	3-Nitro	$\text{BrCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{Br}$	152
	4-Nitro	$\text{BrCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{NO}_2$	228
	2,4-Dibromo	$\text{BrCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{NO}_2$	228
	2,4,6-Trichloro	$\text{BrCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{Br}$	152
	2,4,6-Tribromo	$\text{BrCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{Br}$	230
	2-Bromo-4-nitro	$\text{BrCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{Br}$	230
	2,6-Dibromo-4-nitro	$\text{BrCH}_2\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{Br}$	228
Ethyl 3-oxohexanoate	—	$n\text{-C}_5\text{H}_{11}\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_5$	228
Ethyl 3-oxononanoate	—	$n\text{-C}_7\text{H}_{15}\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_5$	260
Methyl benzoylacetae	—	$n\text{-C}_6\text{H}_{13}\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_5$	260
Ethyl benzoylacetae	—	$\text{C}_6\text{H}_5\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_5$	260
	4-Nitro	$\text{C}_6\text{H}_5\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2$	261, 262
	—	$\text{C}_6\text{H}_5\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_5$ (70)	261, 262
	4-Methyl	$\text{C}_6\text{H}_5\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3$	265, 140,
	2-Nitro	$\text{C}_6\text{H}_5\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{NO}_2$	263, 264
	3-Nitro	$\text{C}_6\text{H}_5\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{NO}_2$	264
	4-Nitro	$\text{C}_6\text{H}_5\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{NO}_2$	263, 266
	4-Acetamido	$\text{C}_6\text{H}_5\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{NHCOCH}_3$	266
	4-Methyl-2-nitro	$\text{C}_6\text{H}_5\text{COC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3$	267

Note: References 177-480 are on pp. 138-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

† This product was obtained when 2 equivalents of the diazonium salt were used.

TABLE II—Continued

B. β -Keto Esters—Continued		Substituent(s) in Aniline*	Product (Yield, %)	References
β -Keto Ester				
Methyl <i>o</i> -methoxybenzoyl- acetate		—	$o\text{-CH}_3\text{OC}_6\text{H}_4\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_5$	268
Methyl <i>m</i> -methoxybenzoyl- acetate		4-Nitro	$o\text{-CH}_3\text{OC}_6\text{H}_4\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	268
		—	$m\text{-CH}_3\text{OC}_6\text{H}_4\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_5$	268
Methyl <i>p</i> -methoxybenzoyl- acetate		4-Nitro	$m\text{-CH}_3\text{OC}_6\text{H}_4\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	268
		—	$p\text{-CH}_3\text{OC}_6\text{H}_4\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_5$	268
Methyl <i>o</i> -chlorobenzoyl- acetate		4-Nitro	$p\text{-CH}_3\text{OC}_6\text{H}_4\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	268
		—	$o\text{-ClC}_6\text{H}_4\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_5$	269
Methyl <i>m</i> -chlorobenzoyl- acetate		4-Nitro	$o\text{-ClC}_6\text{H}_4\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	269
		—	$m\text{-ClC}_6\text{H}_4\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_5$	269
Methyl <i>p</i> -chlorobenzoyl- acetate		4-Nitro	$m\text{-ClC}_6\text{H}_4\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	269
		—	$p\text{-ClC}_6\text{H}_4\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_5$	269
Dimethyl oxalacetate		4-Nitro	$p\text{-ClC}_6\text{H}_4\text{COC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	269
		—	$\text{CH}_3\text{O}_2\text{CCOC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_5$ (40)	62
Diethyl oxalacetate		Benzidine	$[\text{CH}_3\text{O}_2\text{CCOC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_4\text{-}]_2$ (65)	270
		—	$\text{C}_2\text{H}_5\text{O}_2\text{CCOC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_5$ (75)	62, 61
			$\text{C}_6\text{H}_5\text{N}=\text{NC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_5$ † (76)	63, 61
2-Methyl			$\text{C}_2\text{H}_5\text{O}_2\text{CCOC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-}o$	62, 271
			$o\text{-CH}_3\text{C}_6\text{H}_4\text{N}=\text{NC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-}o$ † (81)	63
4-Bromo			$\text{C}_2\text{H}_5\text{O}_2\text{CCOC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{Br-}p$ (92)	66
			$p\text{-BrC}_6\text{H}_4\text{N}=\text{NC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{Br-}p$ † (41)	66
2,4-Dibromo			$\text{C}_2\text{H}_5\text{O}_2\text{CCOC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_3\text{Br}_2\text{-}2,4$	272

Diethyl acetonedicarboxylate	4,4'-Biphenylenedihydrazonobis(diethyl dioxosuccinate) (76)	270, 273
—	3,3'-Dimethyl-4,4'-biphenylenedihydrazonobis(diethyl dioxosuccinate) (60)	273, 270
—	3,3'-Dimethoxy-4,4'-biphenylenedihydrazonobis(diethyl dioxosuccinate) (55-60)	273, 270
—	$C_2H_5O_2CCH_2COC(CO_2C_2H_5)=NNHC_6H_5$ (86)	65, 274
2-Methyl	$C_2H_5O_2CCH_2COC(CO_2C_2H_5)=NNHC_6H_4CH_3-o$ (94)	65
4-Methyl	$C_2H_5O_2CCH_2COC(CO_2C_2H_5)=NNHC_6H_4CH_3-p$ (90)	65
4-Nitro	$C_2H_5O_2CCH_2COC(CO_2C_2H_5)=NNHC_6H_4NO_2-p$	64
2-Carboxy	$C_2H_5O_2CCH_2COC(CO_2C_2H_5)=NNHC_6H_4CO_2H-o$ (70)	65
2,4-Dimethyl	$C_2H_5O_2CCH_2COC(CO_2C_2H_5)=NNHC_6H_3(CH_3)_2-2,4$	65
4-(p-Phenylmercaptobenzoyl)	Diethyl α,β -dioxoglutarate α -[p-(p-phenylmercaptobenzoyl)-phenylhydrazine] (27)	13
4-(3,4-Dicarbethoxy-5-methyl-1-pyrazolyl)	Diethyl α,β -dioxoglutarate α -[p-(3,4-dicarbethoxy-5-methyl-1-pyrazolyl)phenylhydrazine]	253
—	Diethyl α,α -diethyl- β,γ -dioxoglutarate γ -phenylhydrazono	274
Diethyl α,α -diethyl- β -oxoglutarate	5-Hydroxy-3-oxo-2-phenylhydrazono-4-hexenoic acid lactone (80)	275
5-Hydroxy-3-oxo-4-hexenoic acid lactone	$C_6H_5N=NC(CH=CHCO_2C_2H_5)=NNHC_6H_5$ (18)	66
—	$C_6H_5O_2CCOC(CH=CHCO_2C_2H_5)=NNHC_6H_4Br-p$ (65)	66
4-Bromo	p-BrC ₆ H ₄ N=NC(CH=CHCO ₂ C ₂ H ₅)=NNHC ₆ H ₄ Br-p†	66
—	p-BrC ₆ H ₄ N=NC(CO ₂ C ₂ H ₅)=CHC(COCO ₂ C ₂ H ₅)=NNHC ₆ H ₄ Br-p	66
4-Ethoxy	$C_2H_5O_2CCOC(CH=CHCO_2C_2H_5)=NNHC_6H_4OC_2H_5-p$ ¶ (36-43)	66

Note: References 177-480 are on pp. 136-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

† This product was obtained when 2 equivalents of diazonium salt were used.

‡ This product was obtained by coupling in the presence of ammonia.

§ This product was obtained by coupling in alcoholic hydrochloric acid.

¶ This product was obtained by coupling in the presence of sodium carbonate.

TABLE II—Continued

B. β -Keto Esters—Continued			References
Product (Yield, %)	Substituent(s) in Aniline*		
β, β' -Oxaldihydrazonobis(ethyl α, β -dioxobutyrate)	—		278
α, α' -diphenylhydrazone**	—		
β, β' -Mesoxaldihydrazonobis(ethyl α, β -dioxobutyrate)	—		280, 279
$\alpha, \alpha', \alpha''$ -triphenylhydrazone (72)	—		
β, β' -Mesoxaldihydrazonobis(ethyl α, β -dioxobutyrate)	4-Methyl		280
$\alpha, \alpha', \alpha''$ -tri- <i>p</i> -tolylhydrazone (50)			
C. β -Keto Amides			References
Product (Yield, %)	Substituent(s) in Aniline*		
$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_5$	—		281, 282
$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3$ - <i>o</i>	2-Methyl		283
$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3$ - <i>p</i>	4-Methyl		283
$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_4\text{OCH}_3$ - <i>o</i>	2-Methoxy		283
$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_4\text{OCH}_3$ - <i>p</i>	4-Methoxy		283
$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_4\text{OC}_2\text{H}_5$ - <i>p</i>	4-Ethoxy		283
$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_4\text{Cl}$ - <i>m</i>	3-Chloro		283
$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_4\text{Cl}$ - <i>p</i>	4-Chloro		283
$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_4\text{Br}$ - <i>p</i>	4-Bromo		283
$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_4\text{NO}_2$ - <i>o</i>	2-Nitro		283
$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3$ -4- NO_2 -2	4-Methyl-2-nitro		67, 68
$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_4\text{Cl}$ -4- NO_2 -2	4-Chloro-2-nitro		67, 69
$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}(\text{CH}_3)_2$ -2,4,6- NO_2 -3-nitro	2,4,6-Trimethyl-3-nitro		67, 68
$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_7$ - α	α -Naphthylamine		284
			283

β -Naphthylamine	$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4)=\text{NNHC}_6\text{H}_4, \beta$	283
Anhydrotris o-aminobenzaldehyde	$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4)=\text{NNHC}_6\text{H}_4\text{CHO}-o$	285
4-(3,4-Dicarbethoxy-2,5-dimethylpyrrolyl)	α, β -Dioxobutyranilide α -arylhydrazone	286
4-(3,4-Dicarbethoxy-5-methyl-1-pyrazolyl)	α, β -Dioxobutyranilide α -arylhydrazone	253
Benzidine	$\alpha, \alpha'-(4,4'\text{-Biphenylenedihydrazono})\text{bis}-(\alpha, \beta\text{-dioxobutyranilide})$	287
—	$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{CH}_3-o)=\text{NNHC}_6\text{H}_5$	282
Benzidine	$[\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{CH}_3-o)=\text{NNHC}_6\text{H}_4-1_2]$	287
—	$[\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{CH}_3-p)=\text{NNHC}_6\text{H}_5]$	282
Benzidine	$[\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{CH}_3-p)=\text{NNHC}_6\text{H}_4-1_2]$	287
—	$[\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{OCH}_3-o)=\text{NNHC}_6\text{H}_5]$	282
Benzidine	$[\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{OCH}_3-o)=\text{NNHC}_6\text{H}_4-1_2]$	287
—	$[\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{OCH}_3-p)=\text{NNHC}_6\text{H}_5]$	282
Benzidine	$[\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{OCH}_3-p)=\text{NNHC}_6\text{H}_4-1_2]$	287
—	$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{OC}_2\text{H}_5-p)=\text{NNHC}_6\text{H}_5$	282
p (3,4-Dicarbethoxy-2,5-dimethylpyrrolyl)	p -Ethoxy- α, β -dioxobutyranilide α -arylhydrazone	286
Benzidine	$[\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{OC}_2\text{H}_5-p)=\text{NNHC}_6\text{H}_4-1_2]$	287
4-Chloro 2-nitro	$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{Cl}-o)=\text{NNHC}_6\text{H}_4\text{Cl}-4\text{-NO}_2-2$	67, 68
—	$[\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{Cl}-m)=\text{NNHC}_6\text{H}_5]$	283
Benzidine	$[\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{Cl}-m)=\text{NNHC}_6\text{H}_4-1_2]$	287

Note: References 177-180 are on pp. 136-142.

- * The full name is given when it is awkward to name the arylamine as a derivative of aniline.
- ** Some monophenyldiazones was isolated.

TABLE II—Continued

C. β -Keto Amides—Continued

Substituent(s) in Aniline*	Product (Yield, %)	References
β -Keto Amide		
<i>p</i> -Chloroacetacetanilide	$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{Cl-}p)=\text{NNHC}_6\text{H}_5$	282
<i>p</i> -Bromoacetacetanilide	$[\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{Cl-}p)=\text{NNHC}_6\text{H}_4\text{-}l_2]$	287
<i>p</i> -Sulfamylacetacetanilide	$[\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{Br-}p)=\text{NNHC}_6\text{H}_5]$	282
<i>N</i> -(α -Naphthyl)acetacetamide	$[\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{Br-}p)=\text{NNHC}_6\text{H}_4\text{-}l_2]$	287
	$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{SO}_2\text{NH}_2\text{-}p)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}o$	288
	$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{SO}_2\text{NH}_2\text{-}p)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}m$	288
	$\text{CH}_3\text{COC}(\text{CONHC}_6\text{H}_4\text{SO}_2\text{NH}_2\text{-}p)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	288
	$\text{CH}_3\text{COC}(\text{CONHC}_{10}\text{H}_7\text{-}z)=\text{NNHC}_6\text{H}_5$	282
<i>N</i> -(β -Naphthyl)acetacetamide	$[\text{CH}_3\text{COC}(\text{CONHC}_{10}\text{H}_7\text{-}z)=\text{NNHC}_6\text{H}_4\text{-}l_2]$	285
	$\text{CH}_3\text{COC}(\text{CONHC}_{10}\text{H}_7\text{-}\beta)=\text{NNHC}_6\text{H}_5$	282
<i>N,N</i> -Diphenylacetacetamide	$[\text{CH}_3\text{COC}(\text{CONHC}_{10}\text{H}_7\text{-}\beta)=\text{NNHC}_6\text{H}_4\text{-}l_2]$	285
	$(\text{C}_6\text{H}_5)_2\text{NCOC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}o$ (80-90)	288
	$(\text{C}_6\text{H}_5)_2\text{NCOC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}m$ (80-90)	288
	$(\text{C}_6\text{H}_5)_2\text{NCOC}(\text{COCH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$ (80-90)	288
<i>N</i> -Sulfoacetacetamide	$\text{CH}_3\text{COC}(\text{CONHSO}_3\text{H})=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	280
<i>N</i> -Sulfamylacetacetamide	$\text{CH}_3\text{COC}(\text{CONHSO}_2\text{NH}_2)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$	280
Acetacetanilide phenylhydrazone	$\text{CH}_3\text{C}(=\text{NNHC}_6\text{H}_5)\text{C}(=\text{NNHC}_6\text{H}_5)\text{CONHC}_6\text{H}_5$	281
Benzoylacetanilide		
4-Methyl	$\text{C}_6\text{H}_5\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_5$	282
4-Methoxy	$\text{C}_6\text{H}_5\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-}p$	283
4-Ethoxy	$\text{C}_6\text{H}_5\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_4\text{OCH}_3\text{-}p$	283
4-Chloro	$\text{C}_6\text{H}_5\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_4\text{OC}_2\text{H}_5\text{-}p$	283
Benzidine	$[\text{C}_6\text{H}_5\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_4\text{Cl-}p]$	283
	$[\text{C}_6\text{H}_5\text{COC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_4\text{-}l_2]$	287

<i>p</i> -Benzoylacetotoluide	$C_6H_5COC(CONHC_6H_4CH_3-p)=NNHC_6H_5$	282
Benzidine	$[C_6H_5COC(CONHC_6H_4CH_3-p)=NNHC_6H_4-1]$	287
<i>p</i> -Benzoylacetanuide	$C_6H_5COC(CONHC_6H_4OCH_3-p)=NNHC_6H_5$	282
Benzidine	$[C_6H_5COC(CONHC_6H_4OCH_3-p)=NNHC_6H_4-1]$	287
<i>p</i> -Benzoylacetophenetide	$C_6H_5COC(CONHC_6H_4OC_2H_5-p)=NNHC_6H_5$	282
Benzidine	$[C_6H_5COC(CONHC_6H_4OC_2H_5-p)=NNHC_6H_4-1]$	287
<i>N</i> - <i>p</i> -Chlorophenylbenzoylacetamide	$C_6H_5COC(CONHC_6H_4Cl-p)=NNHC_6H_5$	282
Benzidine	$[C_6H_5COC(CONHC_6H_4Cl-p)=NNHC_6H_4-1]$	287

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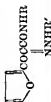
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Reactant,
Substituent R in



Phenyl

Substituents in Product,



R	R'	References
Phenyl	Phenyl	282
Phenyl	<i>o</i> -Tolyl	283
Phenyl	<i>p</i> -Tolyl	283
Phenyl	<i>o</i> -Anisyl	283
Phenyl	<i>p</i> -Anisyl	283
Phenyl	<i>p</i> -Ethoxyphenyl	283
Phenyl	<i>m</i> -Chlorophenyl	283
Phenyl	<i>p</i> -Chlorophenyl	283
Phenyl	<i>p</i> -Bromophenyl	283
Phenyl	α -Naphthyl	283
Phenyl	β -Naphthyl	283
Phenyl	Biphenylene	287

Note: References 177-480 are on pp. 130-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

TABLE II—Continued
C. β -Keto Amides—Continued



Substituents in Product,		References	
Reactant, Substituent R in	Substituent(s) in Aniline	R	R'
 $\text{COCH}_2\text{CONHR}$			 COCCONHR = NNHR'
<i>o</i> -Tolyl	—	<i>o</i> -Tolyl	Phenyl
<i>p</i> -Tolyl	Benzidine	<i>o</i> -Tolyl	Biphenylene
<i>o</i> -Anisyl	—	<i>p</i> -Tolyl	Phenyl
<i>p</i> -Anisyl	Benzidine	<i>p</i> -Tolyl	Biphenylene
	—	<i>o</i> -Anisyl	Phenyl
	Benzidine	<i>o</i> -Anisyl	Biphenylene
	—	<i>p</i> -Anisyl	Phenyl
	Benzidine	<i>p</i> -Anisyl	Biphenylene
<i>p</i> -Ethoxyphenyl	—	<i>p</i> -Ethoxyphenyl	Phenyl
<i>m</i> -Chlorophenyl	Benzidine	<i>p</i> -Ethoxyphenyl	Biphenylene
<i>p</i> -Chlorophenyl	—	<i>m</i> -Chlorophenyl	Phenyl
<i>p</i> -Bromophenyl	Benzidine	<i>m</i> -Chlorophenyl	Biphenylene
α -Naphthyl	—	<i>p</i> -Chlorophenyl	Phenyl
β -Naphthyl	Benzidine	<i>p</i> -Chlorophenyl	Biphenylene
	—	<i>p</i> -Bromophenyl	Phenyl
	Benzidine	<i>p</i> -Bromophenyl	Biphenylene
	—	α -Naphthyl	Phenyl
	Benzidine	α -Naphthyl	Biphenylene
	—	β -Naphthyl	Phenyl
	Benzidine	β -Naphthyl	Biphenylene

TABLE III

COUPLING OF DIAZONIUM SALTS WITH MALONIC ACIDS, ESTERS, AND AMIDES

A. Malonic Acids

Malonic Acid	Substituent(s) in Aniline*	Product (Yield, %)	References
Malonic acid	—	$C_6H_5N=NCH=NNHC_6H_5$ (46)	70
	2-Methoxy	$C_6H_5N=NC(C_6H_5)=NNHC_6H_5$ †	70
	4-Methoxy	$o-CH_3OC_6H_4N=NCH=NNHC_6H_4OCH_3-o$ (67)	290a
	2-Bromo	$p-CH_3OC_6H_4N=NCH=NNHC_6H_4OCH_3-p$	240
	4-Bromo	$o-BrC_6H_4NHN=CHCO_2H$ (30–40)	71
	2-Iodo	$p-BrC_6H_4N=NCH=NNHC_6H_4Br-p$	71, 170a
	2-Nitro	$o-IC_6H_4N=NCH=NNHC_6H_4I-o$ †	71
	3-Nitro	$o-O_2NC_6H_4NHN=CHCO_2H$ (50)§	71, 291
	4-Nitro	$m-O_2NC_6H_4N=NCH=NNHC_6H_4NO_2-m$	240
Malonic acid and sodium nitrite	—	$p-O_2NC_6H_4N=NCH=NNHC_6H_4NO_2-p$ $C_6H_5N=NCH=NOH$	71, 240 71
	2-Methoxy	$o-CH_3OC_6H_4N=NCH=NOH$	71
	2-Chloro	$o-ClC_6H_4N=NCH=NOH$	71
	2,4-Dimethyl	$2,4-(CH_3)_2C_6H_3N=NCH=NOH$	71
	α -Naphthyl	$\alpha-C_{10}H_7N=NCH=NOH$	71
	β -Naphthyl	$\beta-C_{10}H_7N=NCH=NOH$	71
Chloromalonic acid	—	$C_6H_5N=NC(Cl)=NNHC_6H_5$ (40–50)	71
	4-Methyl	$p-CH_3C_6H_4N=NC(Cl)=NNHC_6H_4CH_3-p$ (40–50)	72, 170a
	4-Nitro	$p-O_2NC_6H_4N=NC(Cl)=NNHC_6H_4NO_2-p$	72
	β -Naphthylamine	$\beta-C_{10}H_7N=NC(Cl)=NNHC_{10}H_7-\beta$ (good)	72
Ethylmalonic acid	—	$C_6H_5N=NC(C_2H_5)=NNHC_6H_5$ (quant.)	72, 170a
Allylmalonic acid	4-Methyl	$p-CH_3C_6H_4N=NC(CH_3)=NNHC_6H_4CH_3-p$ (50)	73
Benzylmalonic acid	—	$C_6H_5N=NC(CH_2C_6H_5)=NNHC_6H_5$ (50)	73
Phenacylmalonic acid	—	$C_6H_5N=NC(CH_2COC_6H_5)=NNHC_6H_5$	73 292

B. Malonic Esters		
Malonic Ester	Substituent(s) in Aniline*	Product (Yield, %)
Ethyl hydrogen malonate	4-Nitro	$p\text{-O}_2\text{NC}_6\text{H}_4\text{N}=\text{NC}(\text{CO}_2\text{C}_2\text{H}_5)_2=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$ (52)
	2-Carboxy-4-chloro	$2,4\text{-HO}_2\text{C}(\text{Cl})\text{C}_6\text{H}_3\text{NHN}=\text{CHCO}_2\text{C}_2\text{H}_5$ (52)
	2-Carboxy-5-chloro	$2,5\text{-HO}_2\text{C}(\text{Cl})\text{C}_6\text{H}_3\text{NHN}=\text{CHCO}_2\text{C}_2\text{H}_5$ (79)
	—	$\text{C}_6\text{H}_5\text{NHN}=\text{C}(\text{CO}_2\text{CH}_3)_2$
Dimethyl malonate	2-Methyl	$o\text{-CH}_3\text{C}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{CH}_3)_2$
	3-Methyl	$m\text{-CH}_3\text{C}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{CH}_3)_2$
	4-Methyl	$p\text{-CH}_3\text{C}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{CH}_3)_2$
	2-Methoxy	$o\text{-CH}_3\text{OC}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{CH}_3)_2$
	4-Methoxy	$p\text{-CH}_3\text{OC}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{CH}_3)_2$
	2-Nitro	$o\text{-O}_2\text{NC}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{CH}_3)_2$
	3-Nitro	$m\text{-O}_2\text{NC}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{CH}_3)_2$
	4-Nitro	$p\text{-O}_2\text{NC}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{CH}_3)_2$
	2-Carboxy	$o\text{-HO}_2\text{CC}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{CH}_3)_2$
	3-Carboxy	$m\text{-HO}_2\text{CC}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{CH}_3)_2$
	4-Carboxy	$p\text{-HO}_2\text{CC}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{CH}_3)_2$
	2,4-Dimethyl	$2,4\text{-(CH}_3)_2\text{C}_6\text{H}_3\text{NHN}=\text{C}(\text{CO}_2\text{CH}_3)_2$
	Benidine	$4,4'\text{-Biphenylenedihydrazonobis(dimethyl mesoxalate)}$
		References
		19c
		74a
		74a
		74b, 293
		293
		293
		293
		293
		293
		293
		293
		293
		293
		294, 295

Note: References 177-180 are on pp. 136-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

† This product was obtained when excess diazonium salt was used.

‡ Glyoxylic acid *o*-iodophenylhydrazone was also formed in 8% yield.

§ N,N'-Di-*o*-nitrophenylformazan was also formed in 5% yield.

|| With excess chloromalonate the corresponding 3-aryl-1,3,4-oxadiazol-2-one was formed.

TABLE III—Continued

B. Malonic Esters—Continued

Malonic Ester	Substituent(s) in Aniline*	Product (Yield, %)	References
Dimethyl malonate (Cont.)	3,3'-Dimethyl- benzidine	3,3'-Dimethyl-4,4'-biphenylenedihydrazonobis(dimethyl mesoxalate) (84)	294, 295
	3,3'-Dimethoxy- benzidine	3,3'-Dimethoxy-4,4'-biphenylenedihydrazonobis(dimethyl mesoxalate) (71)	294, 295
Diethyl malonate	—	$C_6H_5NHN=C(CO_2C_2H_5)_2$	8, 74c, 296
	3-Chloro	$m\text{-ClC}_6H_4NHN=C(CO_2C_2H_5)_2$ (78)	74a
	4-Bromo	$p\text{-BrC}_6H_4NHN=C(CO_2C_2H_5)_2$	74c
	4-Nitro	$p\text{-O}_2\text{NC}_6H_4NHN=C(CO_2C_2H_5)_2$ (71)	19c
	3-Carboxy	$m\text{-HO}_2\text{CC}_6H_4NHN=C(CO_2C_2H_5)_2$	242
	4-Phenyl	$p\text{-C}_6H_5\text{C}_6H_4NHN=C(CO_2C_2H_5)_2$ (50)	96
	4-Methoxy-2-nitro	$4\text{-CH}_3\text{O}-2\text{-O}_2\text{NC}_6H_3NHN=C(CO_2C_2H_5)_2$ (47)	74a
	2-Carboxy-5- chloro	$2\text{-HO}_2\text{C}-5\text{-ClC}_6H_3NHN=C(CO_2C_2H_5)_2$ (67)	74a
	Benzidine	4,4'-Biphenylenedihydrazonobis(diethyl mesoxalate)	294
	3,3'-Dimethyl- benzidine	3,3'-Dimethyl-4,4'-biphenylenedihydrazonobis(diethyl mesoxalate) (80)	294
	3,3'-Dimethoxy- benzidine	3,3'-Dimethoxy-4,4'-biphenylenedihydrazonobis(diethyl mesoxalate)	294
	3,3'-Dicarboxy- benzidine	3,3'-Dicarboxy-4,4'-biphenylenedihydrazonobis(diethyl mesoxalate)	242
Diethyl chloromalonate	4-Nitro	$p\text{-O}_2\text{NC}_6H_4N=NCCl(CO_2C_2H_5)_2$ (quant.)	72
Glutaconic acid	—	$C_6H_5N=NCC(CO_2H)=CHCO_2H=NNHC_6H_5$	297
Diethyl glutaconate	—	$C_6H_5NHN=C(CO_2C_2H_5)CH=CHCO_2C_2H_5$ (77)	298, 76
	2-Methyl	$o\text{-CH}_3\text{C}_6H_4NHN=C(CO_2C_2H_5)CH=C(CO_2C_2H_5)N=NC_6H_4CH_3$ (62)	297, 76, 299
		$o\text{-CH}_3\text{C}_6H_4NHN=C(CO_2C_2H_5)CH=C(CO_2C_2H_5)N=NC_6H_4CH_3$ (61)	76

4-Methyl	$p\text{-CH}_3\text{C}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{N}=\text{NC}_6\text{H}_4\text{CH}_3$, <i>p</i> [†]	76
2-Ethoxy	$o\text{-C}_2\text{H}_5\text{OC}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}=\text{CHCO}_2\text{C}_2\text{H}_5$	76
	$o\text{-C}_2\text{H}_5\text{OC}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{N}=\text{NC}_6\text{H}_4\text{OC}_2\text{H}_5$, <i>o</i> [†]	76
4-Chloro	$p\text{-ClC}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{N}=\text{NC}_6\text{H}_4\text{Cl}$, <i>p</i> [†]	76
2-Bromo	$o\text{-BrC}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{N}=\text{NC}_6\text{H}_4\text{Br}$, <i>o</i> [†]	76
3-Bromo	$m\text{-BrC}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{N}=\text{NC}_6\text{H}_4\text{Br}$, <i>m</i> [†]	76
4-Bromo	$p\text{-BrC}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{N}=\text{NC}_6\text{H}_4\text{Br}$, <i>p</i> [†]	76
4-Nitro	$p\text{-O}_2\text{NC}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}=\text{CHCO}_2\text{C}_2\text{H}_5$	76
2,4-Dimethyl	$2,4\text{-(CH}_3)_2\text{C}_6\text{H}_3\text{NHN}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}=\text{CHCO}_2\text{C}_2\text{H}_5$	76
	$2,4\text{-(CH}_3)_2\text{C}_6\text{H}_3\text{NHN}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{N}=\text{NC}_6\text{H}_4\text{(CH}_3)_2$, <i>2,4</i> [†]	76
	$\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{N}=\text{NC}_6\text{H}_4\text{(CH}_3)_2$, <i>2,4</i> [†]	76
2,4,6-Trimethyl	$2,4,6\text{-(CH}_3)_3\text{C}_6\text{H}_2\text{NHN}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}=\text{CHCO}_2\text{C}_2\text{H}_5$	76
	$2,4,6\text{-(CH}_3)_3\text{C}_6\text{H}_2\text{NHN}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{N}=\text{NC}_6\text{H}_4\text{(CH}_3)_3$, <i>2,4,6</i> [†]	76

C. Malonic Amides

Malonic Amide	Substituent in Aniline	Product (Yield, %)	References
Malonamide	—	$\text{C}_6\text{H}_5\text{NHN}=\text{C}(\text{CONH}_2)_2$	75
Diethyl N,N'-malonyl-di-carbamate	—	$\text{C}_6\text{H}_5\text{NHN}=\text{C}(\text{CONHCO}_2\text{C}_2\text{H}_5)_2$ (87)	75
4-Methyl	4-Methyl	$\text{C}_6\text{H}_4\text{NHN}=\text{C}(\text{CONHCO}_2\text{C}_2\text{H}_5)\text{N}=\text{NC}_6\text{H}_4$, ** (74)	75
		$p\text{-CH}_3\text{C}_6\text{H}_4\text{NHN}=\text{C}(\text{CONHCO}_2\text{C}_2\text{H}_5)_2$	75
		$p\text{-ClC}_6\text{H}_4\text{NHN}=\text{C}(\text{CONHCO}_2\text{C}_2\text{H}_5)\text{N}=\text{NC}_6\text{H}_4\text{CH}_3$, **	75

Note: References 177-180 are on pp. 136-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

† This product was obtained when 2 equivalents of diazonium salt were used.

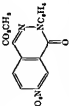
** This product is obtained when 2 equivalents of diazonium salt are used in the presence of sodium carbonate.

TABLE III—Continued

B. Malonic Esters—Continued

Malonic Ester	Substituent(s) in Aniline*	Product (Yield, %)	References
Dimethyl malonate (Cont.)	3,3'-Dimethyl- benzidine	3,3'-Dimethyl-4,4'-biphenylenedihydrazonobis(dimethyl mesoxalate) (84)	294, 295
	3,3'-Dimethoxy- benzidine	3,3'-Dimethoxy-4,4'-biphenylenedihydrazonobis(dimethyl mesoxalate) (71)	294, 295
Diethyl malonate	—	$C_6H_5NHN=C(CO_2C_2H_5)_2$	8, 74c, 296 74a
	3-Chloro	$m\text{-ClC}_6H_4NHN=C(CO_2C_2H_5)_2$ (78)	74c
	4-Bromo	$p\text{-BrC}_6H_4NHN=C(CO_2C_2H_5)_2$	19c
	4-Nitro	$p\text{-O}_2NC_6H_4NHN=C(CO_2C_2H_5)_2$ (71)	242
	3-Carboxy	$m\text{-HO}_2CC_6H_4NHN=C(CO_2C_2H_5)_2$	96
	4-Phenyl	$p\text{-C}_6H_5C_6H_4NHN=C(CO_2C_2H_5)_2$ (50)	74a
	4-Methoxy-2-nitro	$4\text{-CH}_3O\text{-}2\text{-O}_2NC_6H_3NHN=C(CO_2C_2H_5)_2$ (47)	74a
	2-Carboxy-5- chloro	$2\text{-HO}_2C\text{-}5\text{-ClC}_6H_3NHN=C(CO_2C_2H_5)_2$ (67)	74a
	Benzidine	4,4'-Biphenylenedihydrazonobis(diethyl mesoxalate)	294
	3,3'-Dimethyl- benzidine	3,3'-Dimethyl-4,4'-biphenylenedihydrazonobis(diethyl mesoxalate) (80)	294
	3,3'-Dimethoxy- benzidine	3,3'-Dimethoxy-4,4'-biphenylenedihydrazonobis(diethyl mesoxalate)	294
	3,3'-Dicarboxy- benzidine	3,3'-Dicarboxy-4,4'-biphenylenedihydrazonobis(diethyl mesoxalate)	242
Diethyl chloromalonate	4-Nitro	$p\text{-O}_2NC_6H_4N=NCCl(CO_2C_2H_5)_2$ (quant.)	72
Glutaconic acid	—	$C_6H_5N=N\text{-}C(OH=CHCO_2H)=NNHC_6H_5$	297
Diethyl glutaconate	—	$C_6H_5NHN=C(CO_2C_2H_5)CH=CHCO_2C_2H_5$ (77)	298, 76
	2-Methyl	$o\text{-CH}_3C_6H_4NHN=C(CO_2C_2H_5)CH=C(CO_2C_2H_5)N=N\text{-}C_6H_5$ (62)	297, 76, 299
		$o\text{-CH}_3C_6H_4NHN=C(CO_2C_2H_5)CH=C(CO_2C_2H_5)N=N\text{-}C_6H_4CH_3$ (61)	76

TABLE IV
COUPLING OF DIAZONIUM SALTS WITH ARYLACETIC ACIDS AND ESTERS

Acid or Ester	Substituent(s) in Aniline*	Product (Yield, %)	References
2,4 Dinitrophenylacetic acid	—	2,4 (O,N),C ₆ H ₃ C(N=NC ₆ H ₅)=NNHC ₆ H ₅	77
	4 Bromo	2,4 (O,N),C ₆ H ₃ C(N=NC ₆ H ₄ Br <i>p</i>)=NNHC ₆ H ₅ Br <i>p</i>	77
	2,4 Dichloro	2,4 (O,N),C ₆ H ₃ C(N=NC ₆ H ₃ Cl ₂ -2,4)=NNHC ₆ H ₅ Cl ₂ -2,4	77
	2,4 Dibromo	2,4 (O,N),C ₆ H ₃ C(N=NC ₆ H ₃ Br ₂ -2,4)=NNHC ₆ H ₅ Br ₂ -2,4	77
Methyl 2,4 dinitrophenylacetate	—	2,4 (O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅	79, 80, 301
	2 Methyl	2,4-(O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ CH ₃ - <i>o</i> (88)	79
	4 Methyl	2,4-(O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ CH ₃ - <i>p</i> (76)	78, 302
	4-Methoxy	2,4 (O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ OCH ₃ - <i>p</i>	79
	4 Chloro	2,4 (O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ Cl <i>p</i>	77
	4 Bromo	2,4 (O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ Br <i>p</i>	77
	4 Acetyl	2,4 (O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ COCH ₃ - <i>p</i>	78
	2 Nitro	2,4 (O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ NO ₂ - <i>o</i> (30)	79
	3 Nitro	2,4 (O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ NO ₂ - <i>m</i> (15)	79
	4 Nitro	2,4 (O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ NO ₂ - <i>p</i>	79
	2 Carboxy	2,4 (O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ CO ₂ H- <i>o</i> (quant)	79
	4 Carboxy	2,4 (O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ CO ₂ H- <i>p</i> (quant)	78
	4 Sulfo	2,4-(O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ SO ₃ H- <i>p</i>	302
	2,4 Dimethyl	2,4 (O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ (CH ₃) ₂ -2,4	302
	2,4 Dichloro	2,4 (O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ Cl ₂ -2,4 (55)	78, 77
	2,4 Dibromo	2,4 (O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ Br ₂ -2,4	77
	2,4,6-Trimethyl	2,4 (O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ (CH ₃) ₃ -2,4,6 (80)	78
	2,4,6 Trichloro	2,4 (O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ Cl ₃ -2,4,6 (46)	78
	α Naphthyl	2,4 (O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ α	302
	β Naphthyl	2,4 (O,N),C ₆ H ₃ C(CO ₂ CH ₃)=NNHC ₆ H ₅ β	79
Dimethyl 4 nitrohomophthalate	—		79
Methyl 4 carbomethoxy 2 nitrophenylacetate	—	C ₆ H ₃ NHN=C(CO ₂ CH ₃)C ₆ H ₃ CO ₂ CH ₃ -4 NO ₂ -2	79
Homophthalic anhydride	—	α Phenylhydratohomophthalic anhydride	81

* The full name is given when it is awkward to name the arylamine as a derivative of aniline

Note: References 177-180 are on pp 136-142

TABLE III—Continued

C. Malonic Amides—Continued			References
Malonic Amide	Substituent in Aniline	Product (Yield, %)	
Diethyl N,N'-malonyl-dicarbamate (Cont.)	2-Nitro	$o\text{-O}_2\text{NC}_6\text{H}_4\text{NHN}=\text{C}(\text{CONHCO}_2\text{C}_2\text{H}_5)_2$	75
	3-Nitro	$o\text{-O}_2\text{NC}_6\text{H}_4\text{NHN}=\text{C}(\text{CONHCO}_2\text{C}_2\text{H}_5)_2\text{N}=\text{NC}_6\text{H}_4\text{NO}_2\text{-}o^{**}$	75
	4-Nitro	$m\text{-O}_2\text{NC}_6\text{H}_4\text{NHN}=\text{C}(\text{CONHCO}_2\text{C}_2\text{H}_5)_2$	75
Malonamidine	—	$p\text{-O}_2\text{NC}_6\text{H}_4\text{NHN}=\text{C}(\text{CONHCO}_2\text{C}_2\text{H}_5)_2$	75
$\text{CH}_2(\text{CONHN}=\text{C}(\text{CH}_3)\text{-C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_5)_2$	—	$\text{C}_6\text{H}_5\text{NHN}=\text{C}(\text{C}(\text{=NH})\text{NH}_2)_2$	300a
Ethyl malonanilate	—	$\text{C}_6\text{H}_5\text{NHN}=\text{C}(\text{CONHN}=\text{C}(\text{CH}_3)\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_5)_2$	280
Methyl N-(α -pyridyl)malonamate	—	$\text{C}_6\text{H}_5\text{NHN}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{CONHC}_6\text{H}_5$	300b
Ethyl N-(γ -pyridyl)malonamate	—	$\text{C}_6\text{H}_5\text{NHN}=\text{C}(\text{CO}_2\text{CH}_3)\text{CONHC}_3\text{H}_4\text{N-}\alpha$ (quant.)	300b
Malonic acid	4-Nitro	$\text{C}_6\text{H}_5\text{NHN}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{CONHC}_3\text{H}_4\text{N-}\gamma$	300c
Ethyl malonamate	4-Nitro	$p\text{-O}_2\text{NC}_6\text{H}_4\text{N}=\text{NC}(\text{CONH}_2)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-}p$ (89)	19c
	4-Nitro	$p\text{-O}_2\text{NC}_6\text{H}_4\text{NHN}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)\text{CONH}_2$ (36)	19c

Note: References 177–180 are on pp. 136–142.

** This product is obtained when 2 equivalents of diazonium salt are used in the presence of sodium carbonate.

3-Bromo	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{Br-}m$	311
2-Nitro	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{NO}_2-o$	312
3-Nitro	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{NO}_2-m$ (76)	312
4-Nitro	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{NO}_2-p$ (97)	312
2-Carboxy	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CO}_2\text{H } o$	82
3-Carboxy	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CO}_2\text{H-}m$	311
2-Carbomethoxy	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CO}_2\text{CH}_3-o$	310
4-Sulfo	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{SO}_3\text{H-}p$	311
2,4-Dimethyl	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_3(\text{CH}_3)_2-2,4$	82
2,4,5-Trimethyl	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_3(\text{CH}_3)_3-2,4,5$	82
2,4-Dichloro	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_3\text{Cl}_2-2,4$ (98)	313
2,5-Dichloro	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_3\text{Cl}_2-2,5$ (99)	313
2,5-Dibromo	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_3\text{Br}_2-2,5$	311
2,4,6-Tribromo	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_2\text{Br}_3-2,4,6$	311
2 Chloro-4-methyl	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_3\text{Cl-}2\text{-CH}_3-4$ (71)	238
4-Chloro-2-methyl	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_3\text{Cl-}4\text{-CH}_3-2$ (92)	311
α -Naphthylamine	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_{10}\text{H}_7-z$	238
β -Naphthylamine	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_{10}\text{H}_7-\beta$	311
Benzidine	3,3'-Biphenylenedihydrazonobis(ethyl cyanoglyoxalate)	305, 310
3,3'-Dimethyl-benzidine	3,3'-Dimethyl-4,4'-biphenylenedihydrazonobis(ethyl cyanoglyoxalate)	305, 310
3,3'-Dimethoxy-benzidine	3,3'-Dimethoxy-4,4'-biphenylenedihydrazonobis(ethyl cyanoglyoxalate)	305, 310
—	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5-n)=\text{NNHC}_6\text{H}_5$	314
—	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5-n)=\text{NNHC}_6\text{H}_5$	314
—	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_{11-n})=\text{NNHC}_6\text{H}_5$	314
4-Methyl	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5-l)=\text{NNHC}_6\text{H}_4\text{CH}_3-p$	315
4-Bromo	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5-l)=\text{NNHC}_6\text{H}_4\text{Br-p}$	19c
4-Nitro	$\text{CNC}(\text{CONH}_2)=\text{NNHC}_6\text{H}_4\text{NO}_2-p$ (56)	

Notes: References 177-480 are on pp. 136-142
 * The full name is given when it is awkward to name the arylamine as a derivative of aniline.

TABLE V
COUPLING OF DIAZONIUM SALTS WITH NITRILES

Nitrile	Substituent(s) in Aniline*	Product (Yield, %)	References
Cyanoacetaldehyde	—	$\text{CNC}(\text{CHO})=\text{NNHC}_6\text{H}_5$ (15)	86, 85
	4-Bromo	$\text{CNC}(\text{CHO})=\text{NNHC}_6\text{H}_4\text{Br}-p$	86
	4-Nitro	$\text{CNC}(\text{CHO})=\text{NNHC}_6\text{H}_4\text{NO}_2-p$ (11)	19c
Cyanoacetic acid	—	$\text{C}_6\text{H}_5\text{N}=\text{NC}(\text{CN})=\text{NNHC}_6\text{H}_5$	95a
	2-Carboxy	$o\text{-HO}_2\text{C}_6\text{H}_4\text{N}=\text{NC}(\text{CN})=\text{NNHC}_6\text{H}_4\text{CO}_2\text{H}-o$ (65)	303
	4-Nitro	$p\text{-O}_2\text{NC}_6\text{H}_4\text{N}=\text{NC}(\text{CN})=\text{NNHC}_6\text{H}_4\text{NO}_2-p$	19c
Methyl cyanoacetate	2-Hydroxy-5-chloro	$2\text{-HO-5-ClC}_6\text{H}_3\text{N}=\text{NC}(\text{CN})=\text{NNHC}_6\text{H}_3\text{Cl-5-OH-2}$	232a
	—	$\text{CNC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_5$	304
	2-Methyl	$\text{CNC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_4\text{CH}_3-o$	304
	4-Methyl	$\text{CNC}(\text{CO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_4\text{CH}_3-p$	304
	Benzidine	$4,4'\text{-Biphenylenedihydrazonobis(methyl cyanoglyoxalate)}$	304
	3,3'-Dimethyl- benzidine	$3,3'\text{-Dimethyl-4,4'-biphenylenedihydrazonobis(methyl cyanoglyoxalate)}$	305, 306
	3,3'-Dimethoxy- benzidine	$3,3'\text{-Dimethoxy-4,4'-biphenylenedihydrazonobis(methyl cyanoglyoxalate)}$	305, 306
Ethyl cyanoacetate	—	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_5$ (quant.)	305, 306
	2-Methyl	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3-o$	82, 71c, 175,
	4-Methyl	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3-p$	304, 307-309
	2-Methoxy	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{OCH}_3-p$	82, 304
	4-Methoxy	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{OCH}_3-o$	82, 304
	4-Ethoxy	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{OC}_2\text{H}_5-p$	310
	2-Hydroxy	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{OH}-o$	310
	3-Hydroxy	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{OH}-m$	310
	4-Hydroxy	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{OH}-p$	311
	3-Chloro	$\text{CNC}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{Cl}-m$ (97)	311
			71a

2-Carboxy-4-sulfo	$C_6H_4COC(CN)=NNHC_6H_4CO_2H \cdot 2 \cdot SO_3H \cdot 4$	94
2-Hydroxy-4-sulfo-5-methyl	$C_6H_4COC(CN)=NNHC_6H_4OH \cdot 2 \cdot SO_3H \cdot 4 \cdot CH_3 \cdot 5$	94
2-Hydroxy-3-sulfo-5-chloro	$C_6H_4COC(CN)=NNHC_6H_4OH \cdot 2 \cdot SO_3H \cdot 3 \cdot Cl \cdot 5$	94
2-Hydroxy-3-sulfo-5-nitro	$C_6H_4COC(CN)=NNHC_6H_4OH \cdot 2 \cdot SO_3H \cdot 3 \cdot NO_2 \cdot 5$	94
2-Hydroxy-3-carboxy-5-sulfo	$C_6H_4COC(CN)=NNHC_6H_4OH \cdot 2 \cdot CO_2H \cdot 3 \cdot SO_3H \cdot 5$	94
2-Hydroxy-4-sulfo-1-naphthylamine	α, β -Dioxo- β -phenylpropionitrile α -(2-hydroxy-4-sulfo-1-naphthylhydrazine)	94
2-Hydroxy-4-sulfo-6-nitro-1-naphthylamine	α, β -Dioxo- β -phenylpropionitrile α -(2-hydroxy-4-sulfo-6-nitro-1-naphthylhydrazine)	94
2-Hydroxy-4-sulfo-1-naphthylamine	α, β -Dioxo- <i>p</i> -tolylpropionitrile α -(2-hydroxy-4-sulfo-1-naphthylhydrazine)	94
2-Hydroxy-4-sulfo-1-naphthylamine	α, β -Dioxo- <i>o</i> -anisylpropionitrile α -(2-hydroxy-4-sulfo-1-naphthylhydrazine)	94
2-Hydroxy-4-sulfo-1-naphthylamine	α, β -Dioxo- <i>o</i> -ethoxyphenylpropionitrile α -(2-hydroxy-4-sulfo-1-naphthylhydrazine)	94
2-Hydroxy-4-sulfo-1-naphthylamine	α, β -Dioxo- <i>o</i> -propoxyphenylpropionitrile α -(2-hydroxy-4-sulfo-1-naphthylhydrazine)	94
2-Hydroxy-4-sulfo-1-naphthylamine	α, β -Dioxo- <i>o</i> -benzoyloxyphenylpropionitrile α -(2-hydroxy-4-sulfo-1-naphthylhydrazine)	94
2-Hydroxy-4-sulfo-1-naphthylamine	α, β -Dioxo- <i>p</i> -chlorophenylpropionitrile α -(2-hydroxy-4-sulfo-1-naphthylhydrazine)	94

Note: References 177-480 are on pp. 136-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

† Some $p\text{-O}_2\text{NC}_6\text{H}_4\text{N}(\text{CH}_3)\text{N}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ was also formed.

‡ Some $\text{C}_6\text{H}_5\text{N}(\text{C}_6\text{H}_5)\text{N}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ was also formed.

§ Some $p\text{-BrC}_6\text{H}_4\text{N}(\text{C}_2\text{H}_5)\text{N}=\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ was also formed.

TABLE V—Continued
 COUPLING OF DIAZONIUM SALTS WITH NITRILES

Nitrile	Substituent(s) in Aniline*	Product (Yield, %)	References
Cyanoacetanilide	4-Methoxy-2-nitro	$\text{CNC}(\text{CONHC}_6\text{H}_5)=\text{NNHC}_6\text{H}_5\text{OCH}_3\cdot 4\cdot\text{NO}_2\cdot 2$	74a
Ethyl α -cyanopropionate	4-Nitro	$p\text{-O}_2\text{NC}_6\text{H}_4\text{N}=\text{NC}(\text{CH}_3)(\text{CN})\text{CO}_2\text{C}_2\text{H}_5\uparrow$	99
Ethyl α -cyanobutyrate	—	$\text{C}_6\text{H}_5\text{N}=\text{NC}(\text{C}_2\text{H}_5)(\text{CN})\text{CO}_2\text{C}_2\text{H}_5\uparrow$	99
Ethyl cyanopyruvate	4-Bromo	$p\text{-BrC}_6\text{H}_4\text{N}=\text{NC}(\text{C}_2\text{H}_5)(\text{CN})\text{CO}_2\text{C}_2\text{H}_5\uparrow$	99
Malononitrile	—	$\text{C}_6\text{H}_5\text{NHN}=\text{C}(\text{CN})\text{COCO}_2\text{C}_2\text{H}_5\cdot (72)$	80, 87
—	4-Bromo	$p\text{-BrC}_6\text{H}_4\text{NHN}=\text{C}(\text{CN})\text{COCO}_2\text{C}_2\text{H}_5\cdot (83)$	86, 87
—	—	$\text{C}_6\text{H}_5\text{NHN}=\text{C}(\text{CN})_2$	74b, 83
Benzylmalononitrile	4-Nitro	$p\text{-O}_2\text{NC}_6\text{H}_4\text{NHN}=\text{C}(\text{CN})_2\cdot (75)$	84, 19c
—	—	$\text{C}_6\text{H}_5\text{N}=\text{NC}(\text{CN})\text{CH}_2\text{C}_6\text{H}_5\cdot (81)$	99
—	4-Nitro	$p\text{-O}_2\text{NC}_6\text{H}_4\text{N}=\text{NC}(\text{CN})\text{CH}_2\text{C}_6\text{H}_5\cdot (87)$	99
—	4-Phenyl	$p\text{-C}_6\text{H}_5\text{C}_6\text{H}_4\text{N}=\text{NC}(\text{CN})\text{CH}_2\text{C}_6\text{H}_5\cdot (87)$	99
Nitroacetoneitrile	—	$\text{C}_6\text{H}_5\text{NHN}=\text{C}(\text{NO}_2)\text{CN}$	88, 89
Methylsulfinylacetoneitrile	4-Nitro	$p\text{-O}_2\text{NC}_6\text{H}_4\text{NHN}=\text{C}(\text{NO}_2)\text{CN}\cdot (59)$	19c
Methylsulfonylacetonitrile	4-Nitro	$p\text{-O}_2\text{NC}_6\text{H}_4\text{N}=\text{NC}(\text{CN})=\text{NNHC}_6\text{H}_4\text{NO}_2\cdot p\cdot (72)$	19c
p-Nitrophenylacetoneitrile	4-Nitro	$p\text{-O}_2\text{NC}_6\text{H}_4\text{NHN}=\text{C}(\text{CN})\text{SO}_2\text{CH}_3\cdot (63)$	19c
β -Iminobutyronitrile	—	$p\text{-O}_2\text{NC}_6\text{H}_4\text{C}(\text{CN})=\text{NNHC}_6\text{H}_5$	316
β -Oximino-butyronitrile	—	$\text{CH}_3\text{COC}(\text{CN})=\text{NNHC}_6\text{H}_5$	90
β -Iminovaleronitrile	—	$\text{CH}_3\text{COC}(\text{CN})=\text{NNHC}_6\text{H}_5$	90
β -Imino- β -phenyl-propionitrile	—	?	90
β -Phenyliminobutyronitrile	—	$\text{C}_6\text{H}_5\text{COC}(\text{CN})=\text{NNHC}_6\text{H}_5$	90
Benzoylacetonitrile	—	$\text{C}_6\text{H}_5\text{N}=\text{C}(\text{CH}_3)\text{C}(\text{CN})=\text{NNHC}_6\text{H}_5$	91
—	—	$\text{C}_6\text{H}_5\text{COC}(\text{CN})=\text{NNHC}_6\text{H}_5$	317
2-Methyl	—	$\text{C}_6\text{H}_5\text{COC}(\text{CN})=\text{NNHC}_6\text{H}_4\text{CH}_3\cdot o$	317
2-Hydroxy-5-sulfo	—	$\text{C}_6\text{H}_5\text{COC}(\text{CN})=\text{NNHC}_6\text{H}_4\text{OH}\cdot 2\cdot\text{SO}_3\text{H}\cdot 5$	91

2-Hydroxy-4-sulfo- 8-nitro-1- naphthylamine	α,β -Dioxo-3 methoxy-2-naphthylpropionitrile α -(2-hydroxy-4-sulfo-8-nitro-1-naphthylhydrazine)	94
2-Hydroxy-3-nitro- 4-sulfo	α,β -Dioxo-3-methoxy-2-naphthylpropionitrile α -(2 hydroxy-3-nitro-4-sulfophenylhydrazine)	94
2-Hydroxy-4-sulfo- 1-naphthylamine	α,β -Dioxo- β -(5,6,7,8 tetrahydro-2-naphthyl) propionitrile α -(2-hydroxy-4-sulfo 1 naphthylhydrazine)	94
2-Hydroxy-4 sulfo- 1-naphthylamine	α,β -Dioxo β -(5-acenaphthyl)propionitrile α -(2-hydroxy-4-sulfo- 1-naphthyl hydrazine)	94
2-Hydroxy-4-sulfo- 1-naphthylamine	α,β -Dioxo- β -(2-thienyl)propionitrile α (2-hydroxy-4-sulfo-1- naphthylhydrazine)	94
2-Hydroxy-4-sulfo- 1-naphthylamine	α,β -Dioxo- β -(2-furyl)propionitrile α -(2-hydroxy-4-sulfo-1- naphthylhydrazine)	94
2 Carboxy-4 sulfo	α,β -Dioxo- β (2-furyl)propionitrile α -(2-carboxy-4- sulphophenylhydrazine)	94
2-Carboxy-3-sulfo- 4-chloro	α,β -Dioxo- β -(2-furyl)propionitrile α -(2-carboxy-3-sulfo-4- chlorophenylhydrazine)	94
2-Hydroxy-4-sulfo- 8-nitro-1- naphthylamine	α,β -Dioxo- β -(2-furyl)propionitrile α -(2-hydroxy-4-sulfo-6- nitro-1-naphthylhydrazine)	94
2-Carboxy-4-sulfo	4,4'-Biphenylenebis-(α,β -dioxopropionitrile) α,α' -di-(2-carboxy-4-sulfophenylhydrazine)	94
4,4'-Biphenyldicarbonyl- acetonitrile	$C_6H_5SO_2C(CN)=NNHC_6H_5$ $C_6H_5SO_2C(CN)=NNHC_6H_4CH_3$ $C_6H_5SO_2C(CN)=NNHC_6H_4CH_3$ $C_6H_5SO_2C(CN)=NNHC_6H_4OCH_3$ $C_6H_5SO_2C(CN)=NNHC_6H_4OCH_3$	92 92 92 92 92
Phenylsulfonylacetonitrile	—	92

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

TABLE V—Continued
COUPLING OF DIAZONIUM SALTS WITH NITRILES

Nitrile	Substituent(s) in Aniline*	Product (Yield, %)	References
<i>m</i> -Aminobenzoyl- acetonitrile	2-Hydroxy-4-sulfo- 1-naphthylamine	α,β -Dioxo- <i>m</i> -aminophenylpropionitrile α -(2-hydroxy-4-sulfo- 1-naphthylhydrazine)	94
<i>m</i> -Nitrobenzoyl- acetonitrile	2-Hydroxy-4-sulfo- 1-naphthylamine	α,β -Dioxo- <i>m</i> -nitrophenylpropionitrile α -(2-hydroxy-4-sulfo-1- naphthylhydrazine)	94
<i>m</i> -Carboxybenzoyl- acetonitrile	2-Hydroxy-4-sulfo- 1-naphthylamine	α,β -Dioxo- <i>m</i> -carboxyphenylpropionitrile α -(2-hydroxy-4- sulfo-1-naphthylhydrazine)	94
2,4-Dimethoxybenzoyl- acetonitrile	2-Hydroxy-4-sulfo- 1-naphthylamine	α,β -Dioxo-2,4-dimethoxyphenylpropionitrile α -(2-hydroxy- 4-sulfo-1-naphthylhydrazine)	94
3,4-Dichlorobenzoyl- acetonitrile	2-Hydroxy-4-sulfo- 1-naphthylamine	α,β -Dioxo-3,4-dichlorophenylpropionitrile α -(2-hydroxy- 4-sulfo-1-naphthylhydrazine)	94
3,4,5-Trimethoxybenzoyl- acetonitrile	2-Hydroxy-4-sulfo- 1-naphthylamine	α,β -Dioxo-3,4,5-trimethoxyphenylpropionitrile	94
3,4,5-Triethoxybenzoyl- acetonitrile	2-Hydroxy-4-sulfo- 1-naphthylamine	α -(2-hydroxy-4-sulfo-1-naphthylhydrazine)	94
<i>p</i> -(<i>p</i> -Cyanoacetophenyl)- benzoylacetoneitrile	2-Hydroxy-4-sulfo- 1-naphthylamine	α,β -Dioxo-3,4,5-triethoxyphenylpropionitrile	94
Hexahydrobenzoyl- acetonitrile	2-Hydroxy-4-sulfo- 1-naphthylamine	α -(2-hydroxy-4-sulfo-1-naphthylhydrazine)	94
α -Naphthoylacetoneitrile	2-Hydroxy-4-sulfo- 1-naphthylamine	α,β -Dioxocyclohexylpropionitrile α -(2-hydroxy-4-sulfo- 1-naphthylhydrazine)	94
β -Naphthoylacetoneitrile	2-Hydroxy-4-sulfo- 1-naphthylamine	α,β -Dioxo-1-naphthylpropionitrile α -(2-hydroxy-4-sulfo- 1-naphthylhydrazine)	94
3-Methoxy-2-naphthoyl- acetonitrile	2-Hydroxy-4-sulfo- 1-naphthylamine	α,β -Dioxo-2-naphthylpropionitrile α -(2-hydroxy-4-sulfo- 1-naphthylhydrazine)	94
	2-Hydroxy-4-sulfo- 1-naphthylamine	α,β -Dioxo-3-methoxy-2-naphthylpropionitrile	94
	2-Hydroxy-4-sulfo- 1-naphthylamine	α -(2-hydroxy-4-sulfo-1-naphthylhydrazine)	94

β -Naphthylsulfonyl-acetonitrile	—	β -C ₁₀ H ₇ SO ₂ C(CN)=NNHC ₆ H ₄	93
3-Methyl	—	β -C ₁₀ H ₇ SO ₂ C(CN)=NNHC ₆ H ₄ CH ₃ ^m	93
4-Methyl	—	β -C ₁₀ H ₇ SO ₂ C(CN)=NNHC ₆ H ₄ CH ₃ ^p	93
4-Ethoxy	—	β -C ₁₀ H ₇ SO ₂ C(CN)=NNHC ₆ H ₄ OC ₂ H ₅ ^p	93
α -Phenylsulfonylpropionitrile	—	C ₆ H ₅ SO ₂ C(CN)(CH ₃)N=NC ₆ H ₅	93
4-Methyl	—	C ₆ H ₅ SO ₂ C(CN)(CH ₃)N=NC ₆ H ₄ CH ₃ ^p	93
4-Methoxy	—	C ₆ H ₅ SO ₂ C(CN)(CH ₃)N=NC ₆ H ₄ OCH ₃ ^p	93
4-Ethoxy	—	C ₆ H ₅ SO ₂ C(CN)(CH ₃)N=NC ₆ H ₄ OC ₂ H ₅ ^p	93
α -p-Chlorophenylsulfonyl-propionitrile	—	p-ClC ₆ H ₄ SO ₂ C(CN)(CH ₃)N=NC ₆ H ₅	93
β -Naphthylamine	—	p-ClC ₆ H ₄ SO ₂ C(CN)(CH ₃)N=NC ₆ H ₄ ^p	93
α -p-Bromophenylsulfonyl-propionitrile	—	p-BrC ₆ H ₄ SO ₂ C(CN)(CH ₃)N=NC ₆ H ₄ CH ₃ ^p	93
α -(β -Naphthylsulfonyl)-propionitrile	—	p-BrC ₆ H ₄ SO ₂ C(CN)(CH ₃)N=NC ₆ H ₄ OCH ₃ ^p	93
α -(β -Naphthylsulfonyl)-phenylpropionitrile	—	β -C ₁₀ H ₇ SO ₂ C(CN)(CH ₃)N=NC ₆ H ₅	93
α -Phenoxyacetyl- β -imino- β -phenylpropionitrile	—	β -C ₁₀ H ₇ SO ₂ C(CN)(CH ₃)N=NC ₆ H ₄ CH ₃ ^p	93
β -Phenoxyacetimido- β -phenylpropionitrile	—	C ₆ H ₅ OCH ₂ COC(CN)(N=NC ₆ H ₄)C(=NH)C ₆ H ₅	318
	—	C ₆ H ₅ OCH ₂ CON=C(C ₆ H ₅)C(CN)=NNHC ₆ H ₅	319

Note: References 177-480 are on pp. 133-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

TABLE V—Continued
COUPLING OF DIAZONIUM SALTS WITH NITRILES

Nitrile	Substituent(s) in Aniline*	Product (Yield, %)	References
Phenylsulfonylacetonitrile (Cont.)	4-Ethoxy	$C_6H_5SO_2C(CN)=NNHC_6H_4OC_2H_5$, <i>p</i>	92
<i>p</i> -Tolylsulfonylacetonitrile	2,4-Dimethyl	$C_6H_5SO_2C(CN)=NNHC_6H_3(CH_3)_2$, <i>4</i>	92
	—	p -CH ₃ C ₆ H ₄ SO ₂ C(CN)=NNHC ₆ H ₅	92
	2-Methyl	p -CH ₃ C ₆ H ₄ SO ₂ C(CN)=NNHC ₆ H ₄ CH ₃ , <i>o</i>	92
	3-Methyl	p -CH ₃ C ₆ H ₄ SO ₂ C(CN)=NNHC ₆ H ₄ CH ₃ , <i>m</i>	92
	4-Methyl	p -CH ₃ C ₆ H ₄ SO ₂ C(CN)=NNHC ₆ H ₄ CH ₃ , <i>p</i>	92
	2-Methoxy	p -CH ₃ C ₆ H ₄ SO ₂ C(CN)=NNHC ₆ H ₄ OCH ₃ , <i>o</i>	92
	4-Methoxy	p -CH ₃ C ₆ H ₄ SO ₂ C(CN)=NNHC ₆ H ₄ OCH ₃ , <i>p</i>	92
	4-Ethoxy	p -CH ₃ C ₆ H ₄ SO ₂ C(CN)=NNHC ₆ H ₄ OC ₂ H ₅ , <i>p</i>	92
	2,4-Dimethyl	p -CH ₃ C ₆ H ₄ SO ₂ C(CN)=NNHC ₆ H ₃ (CH ₃) ₂ , <i>4</i>	92
	—	p -BrC ₆ H ₄ SO ₂ C(CN)=NNHC ₆ H ₅	93
<i>p</i> -Bromophenylsulfonyl- acetonitrile	4-Ethoxy	p -BrC ₆ H ₄ SO ₂ C(CN)=NNHC ₆ H ₄ OC ₂ H ₅ , <i>p</i>	93
α -Naphthylsulfonyl- acetonitrile	—	α -C ₁₀ H ₇ SO ₂ C(CN)=NNHC ₆ H ₅ (97)	93
	2-Methyl	α -C ₁₀ H ₇ SO ₂ C(CN)=NNHC ₆ H ₄ CH ₃ , <i>o</i>	93
	4-Methyl	α -C ₁₀ H ₇ SO ₂ C(CN)=NNHC ₆ H ₄ CH ₃ , <i>p</i>	93
	4-Methoxy	α -C ₁₀ H ₇ SO ₂ C(CN)=NNHC ₆ H ₄ OCH ₃ , <i>p</i>	93

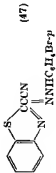
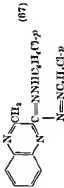
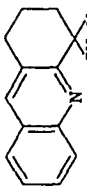
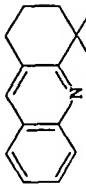
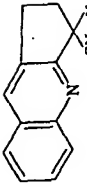
Nitrile	Substituent in Aniline	Product (Yield, %)	References
Benzothiazole-2-acetonitrile	4-Bromo	 (47)	36a
3-Methylquinoxaline-2-acetonitrile	4-Chloro	 (67)	36a

TABLE V—Continued
COUPLING OF DIAZONIUM SALTS WITH NITRILES

Nitrile	Substituent in Aniline	$\begin{array}{c} \text{N}=\text{R}' \\ \diagup \quad \diagdown \\ \text{NCC}=\text{O} \quad \text{O}-\text{N} \\ \parallel \\ \text{RHNN} \end{array}$		Yield, %	References
		R = Phenyl	R' = <i>p</i> -Tolyl		
(3- <i>p</i> -Tolyl-1,2,4-oxadiazol-5-yl)- acetoneitrile	2-Methoxy	R = <i>o</i> -Anisyl	R' = <i>p</i> -Tolyl	20	32
	4-Nitro	R = <i>p</i> -Nitrophenyl	R' = <i>p</i> -Tolyl	20	32
	4-Diethylamino	R = <i>p</i> -Diethylaminophenyl	R' = <i>p</i> -Tolyl	20	32
	4-Diethylamino	R = <i>p</i> -Diethylaminophenyl	R' = <i>m</i> -Nitrophenyl	20	32
(3- <i>m</i> -Nitrophenyl-1,2,4-oxa- diazol-5-yl)acetoneitrile 1,2,3,4-Tetrahydroacridine- 4-carbonitrile	4-Methoxy		CN N=NC ₆ H ₄ OCH ₃ - <i>p</i>	50	98
	4-Bromo		CN N=NC ₆ H ₄ Br- <i>p</i>	56	98
2,3-Dihydro-1-cyclopenta[<i>b</i>]- quinoline-3-carbonitrile	4-Bromo		CN N=NC ₆ H ₄ Br- <i>p</i>	61	98

—	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_5$	92
2-Methyl	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-o}$	92
3-Methyl	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-m}$	92
4-Methyl	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-p}$	92
2-Methoxy	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{OCH}_3\text{-o}$	92
4-Methoxy	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{OCH}_3\text{-p}$	92
4-Ethoxy	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{OC}_2\text{H}_5\text{-p}$	92
2,4-Dimethyl	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_3(\text{CH}_3)_2\text{-2,4}$	92
—	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{CONH}_2)=\text{NNHC}_6\text{H}_5$	92
2-Methyl	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{CONH}_2)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-o}$	92
3-Methyl	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{CONH}_2)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-m}$	92
4-Methyl	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{CONH}_2)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-p}$	92
2-Methoxy	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{CONH}_2)=\text{NNHC}_6\text{H}_4\text{OCH}_3\text{-o}$	92
4-Methoxy	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{CONH}_2)=\text{NNHC}_6\text{H}_4\text{OCH}_3\text{-p}$	92
4-Ethoxy	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{CONH}_2)=\text{NNHC}_6\text{H}_4\text{OC}_2\text{H}_5\text{-p}$	92
2,4-Dimethyl	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{CONH}_2)=\text{NNHC}_6\text{H}_3(\text{CH}_3)_2\text{-2,4}$	92
—	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{CONH}_2)=\text{NNHC}_6\text{H}_5$	92
2-Methyl	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{CONH}_2)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-o}$	92
3-Methyl	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{CONH}_2)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-m}$	92
4-Methyl	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{CONH}_2)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-p}$	92
2-Methoxy	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{CONH}_2)=\text{NNHC}_6\text{H}_4\text{OCH}_3\text{-o}$	92
4-Methoxy	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{CONH}_2)=\text{NNHC}_6\text{H}_4\text{OCH}_3\text{-p}$	92
4-Ethoxy	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{CONH}_2)=\text{NNHC}_6\text{H}_4\text{OC}_2\text{H}_5\text{-p}$	92
2,4-Dimethyl	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{CONH}_2)=\text{NNHC}_6\text{H}_3(\text{CH}_3)_2\text{-2,4}$	92
—	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_5$	102
4-Nitro	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-p (22)}$	10c

Note: References 177-180 are on pp. 130-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

† In addition, some 5-hydroxy-1,3-bis-(*p*-nitrophenyl)tetrazolium betaine was formed.

Ethyl *p* tolylsulfonylacetate

Phenylsulfonylacetamide

p-Tolylsulfonylacetamide

Phenylsulfonylnitromethane
p-Tolylsulfonylnitromethane

TABLE VI
COUPLING OF DIAZONIUM SALTS WITH SULFONES

Sulfone	Substituent(s) in Aniline*	Product (Yield, %)	References
Bis(methylsulfonyl)methane	—	$(\text{CH}_3\text{SO}_2)_2\text{C}=\text{NNHC}_6\text{H}_5$ (56)	101
	2-Methyl	$(\text{CH}_3\text{SO}_2)_2\text{C}=\text{NNHC}_6\text{H}_4\text{CH}_3$ -o (43)	101
	4-Methyl	$(\text{CH}_3\text{SO}_2)_2\text{C}=\text{NNHC}_6\text{H}_4\text{CH}_3$ -p (36)	101
	4-Nitro	$(\text{CH}_3\text{SO}_2)_2\text{C}=\text{NNHC}_6\text{H}_4\text{NO}_2$ -p†	19c
Bis(ethylsulfonyl)methane	—	$(\text{C}_2\text{H}_5\text{SO}_2)_2\text{C}=\text{NNHC}_6\text{H}_5$ (43)	101
	2-Methyl	$(\text{C}_2\text{H}_5\text{SO}_2)_2\text{C}=\text{NNHC}_6\text{H}_4\text{CH}_3$ -o (48)	101
	4-Methyl	$(\text{C}_2\text{H}_5\text{SO}_2)_2\text{C}=\text{NNHC}_6\text{H}_4\text{CH}_3$ -p (33)	101
	4-Nitro	$(\text{C}_2\text{H}_5\text{SO}_2)_2\text{C}=\text{NNHC}_6\text{H}_4\text{NO}_2$ -p†	19c
Methyl (methylsulfonyl)methyl sulfoxide	4-Nitro	$p\text{-O}_3\text{NC}_6\text{H}_4\text{N}=\text{NC}(\text{SO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2$ -p†	19c
Ethyl methylsulfonylacetate	4-Nitro	$\text{CH}_3\text{SO}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{NO}_2$ -p (79)	19c
2-(Methylsulfonyl)acetamide	4-Nitro	$p\text{-O}_3\text{NC}_6\text{H}_4\text{N}=\text{NC}(\text{SO}_2\text{CH}_3)=\text{NNHC}_6\text{H}_4\text{NO}_2$ -p (54)	19c
Methyl nitromethyl sulfone	4-Nitro	$\text{CH}_3\text{SO}_2\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_4\text{NO}_2$ -p (35)	19c
Bis(phenylsulfonyl)methane	4-Nitro	$(\text{C}_6\text{H}_5\text{SO}_2)_2\text{C}=\text{NNHC}_6\text{H}_4\text{NO}_2$ -p†	19c
Bis(methylsulfonyl)methylthiomethane	—	$(\text{CH}_3\text{SO}_2)_2\text{C}(\text{SCH}_3)\text{N}=\text{NC}_6\text{H}_5$ (66)	320
Phenylsulfonylacetic acid	2-Methyl	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{N}=\text{NC}_6\text{H}_4\text{CH}_3\text{-o})=\text{NNHC}_6\text{H}_4\text{CH}_3$ -o	92
	2-Methoxy	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{N}=\text{NC}_6\text{H}_4\text{OCH}_3\text{-o})=\text{NNHC}_6\text{H}_4\text{OCH}_3$ -o	92
	—	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_5$	92
Ethyl phenylsulfonylacetato	2-Methyl	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3$ -o	92
	3-Methyl	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3$ -m	92
	4-Methyl	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{CH}_3$ -p	92
	2-Methoxy	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{OCH}_3$ -o	92
	4-Methoxy	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{OCH}_3$ -p	92
	4-Ethoxy	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_4\text{OC}_2\text{H}_5$ -p	92
2,4-Dimethyl	2,4-Dimethyl	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)=\text{NNHC}_6\text{H}_3(\text{CH}_3)_2$ -2,4	92

TABLE VI—*Continued*
COUPLING OF DIAZONIUM SALTS WITH SULFONES

Sulfone	Substituent(s) in Aniline*	Product (Yield, %)	References
<i>p</i> -Bromophenylsulfonylnitromethane	—	$p\text{-BrC}_6\text{H}_4\text{SO}_2\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_5$	102
<i>m</i> -Nitrobenzyl phenyl sulfone	—	$m\text{-O}_2\text{NC}_6\text{H}_4\text{C}(\text{SO}_2\text{C}_6\text{H}_5)=\text{NNHC}_6\text{H}_5$	102
Sulfazone, i.e.,	5-Sulfo-1-naphthylamine	2-(5-Sulfo-1-naphthylazo)sulfazone	103
	8-Hydroxy-6-sulfo-1-naphthylamine	2-(8-Hydroxy-6-sulfo-1-naphthylazo)sulfazone	103
	3-Sulfo-4-(<i>p</i> -sulphophenylazo)sulfo-1-naphthylamine	2-[3-Sulfo-4-(<i>p</i> -sulphophenylazo)phenylazo]sulfazone	103
	4-[<i>p</i> -(4-Hydroxy-3-carboxyphenylazo)-phenyl] 4-Sulfo	2-[<i>p</i> -(4-Hydroxy-3-carboxyphenylazo)-phenyl]-phenylazo]sulfazone	103
Sulfazone-7-sulfonylacetie acid		2-(<i>p</i> -Sulphophenylazo)sulfazone-7-sulfonylacetie acid	321
	3-Carboxy-4-hydroxy	2-(3-Carboxy-4-hydroxyphenylazo)sulfazone-7-sulfonylacetie acid	321
	4-Sulfo-1-naphthylamine	2-(4-Sulfo-1-naphthylazo)sulfazone-7-sulfonylacetie acid	321

Note: References 177-480 are on pp. 136-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

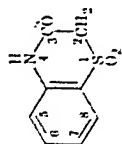


TABLE VII
COUPLING OF DIAZONIUM SALTS WITH NITRO COMPOUNDS

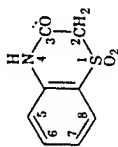
Nitro Compound	Substituent(s) in Aniline*	Product (Yield, %)	References
Nitromethane	—	$C_6H_5NHN=NCHNO_2$	104, 105, 107, 322 20, 3, 104- 107, 323
		$C_6H_5N=NCHNO_2$ $NNHC_6H_5$ (50)	106
2-Methyl		$o\text{-CH}_3C_6H_4N=NCHNO_2$ $NNHC_6H_4CH_3$ o	106
4-Methyl		$p\text{-CH}_3C_6H_4N=NCHNO_2$ $NNHC_6H_4CH_3$ p	20
2-Ethoxy		$o\text{-C}_2H_5OC_6H_4N=NCHNO_2$ $NNHC_6H_4OC_2H_5$ o	106
4-Bromo		$p\text{-BrC}_6H_4N=NCHNO_2$ $NNHC_6H_4Br$ p	322a, 322b
2-Nitro		$o\text{-O}_2NC_6H_4NHN=NCHNO_2$ (77)	106
4-Nitro		$p\text{-O}_2NC_6H_4N=NCHNO_2$ $NNHC_6H_4NO_2$ p	106
2-Formyl		$p\text{-O}_2NC_6H_4NHN=NCHNO_2$ (6)	171, 324
2-Acetyl		$o\text{-HCO}_2C_6H_4NHN=NCHNO_2$ (57)	167d
2-Carboxy		$o\text{-CH}_3CO_2C_6H_4NHN=NCHNO_2$ (64)	167d
2-Carbomethoxy		$o\text{-HOC}_6H_4NHN=NCHNO_2$ (73)	167d
4-Carbomethoxy		$o\text{-CH}_3O_2CC_6H_4NHN=NCHNO_2$ (65)	167d
4-Sulfo		$p\text{-C}_6H_4O_2CC_6H_4NHN=NCHNO_2$ (80)	171
4-Sulfamyl		$p\text{-HOC}_6H_4N=NCHNO_2$ $NNHC_6H_4SO_2H$ p	325
2,4-Dimethyl		$p\text{-H}_2NSO_2C_6H_3N=NCHNO_2$ $NNHC_6H_3SO_2NH_2$ p	106
2-Phenyl		$2,4\text{-C}_6H_3(C_6H_5)_2N=NCHNO_2$ $NNHC_6H_3(C_6H_5)_2$ 2,4 (20)	170
3-Phenyl		$o\text{-C}_6H_4C_6H_4N=NCHNO_2$ $NNHC_6H_4C_6H_5$ o	20
4-Phenyl		$m\text{-C}_6H_4C_6H_4N=NCHNO_2$ $NNHC_6H_4C_6H_5$ m	20
4-Phenoxy		$p\text{-C}_6H_4C_6H_4N=NCHNO_2$ $NNHC_6H_4C_6H_5$ p	106
		$p\text{-C}_6H_4OC_6H_4N=NCHNO_2$ $NNHC_6H_4OC_6H_5$ p	20

Note: References 177-480 are on pp. 130-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

TABLE VI—Continued
COUPLING OF DIAZONIUM SALTS WITH SULFONES

Sulfone	Substituent(s) in Aniline*	Product (Yield, %)	References
<i>p</i> -Bromophenylsulfonylnitromethane	—	$p\text{-BrC}_6\text{H}_4\text{SO}_2\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_5$	102
<i>m</i> -Nitrobenzyl phenyl sulfone	—	$m\text{-O}_2\text{NC}_6\text{H}_4\text{C}(\text{SO}_2\text{C}_6\text{H}_5)=\text{NNHC}_6\text{H}_5$	102
Sulfazone, i.e.,	5-Sulfo-1-naphthylamine	2-(5-Sulfo-1-naphthylazo)sulfazone	103
	8-Hydroxy-6-sulfo-1-naphthylamine	2-(8-Hydroxy-6-sulfo-1-naphthylazo)sulfazone	103
	3-Sulfo-4-(<i>p</i> -sulphenylazo)naphthylamine	2-[3-Sulfo-4-(<i>p</i> -sulphenylazo)phenylazo]sulfazone	103
	4-[<i>p</i> -(4-Hydroxy-3-carboxyphenylazo)-phenyl]	2-[<i>p</i> -(4-Hydroxy-3-carboxyphenylazo)-phenyl]-sulfazone	103
Sulfazone-7-sulfonylacetic acid	4-Sulfo	2-(<i>p</i> -Sulphenylazo)sulfazone-7-sulfonylacetic acid	321
	3-Carboxy-4-hydroxy	2-(3-Carboxy-4-hydroxyphenylazo)sulfazone-7-sulfonylacetic acid	321
	4-Sulfo-1-naphthylamine	2-(4-Sulfo-1-naphthylazo)sulfazone-7-sulfonylacetic acid	321



Note: References 177-180 are on pp. 136-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

TABLE VII—Continued
COUPLING OF DIAZONIUM SALTS WITH NITRO COMPOUNDS

Nitro Compound	Substituent(s) in Aniline*	Product (Yield, %)	References
Nitromethane (Cont.)	α -Naphthylamine	α -C ₁₀ H ₇ N=NC(NO ₂)=NNHC ₁₀ H ₇ - α	106
	β -Naphthylamine	β -C ₁₀ H ₇ N=NC(NO ₂)=NNHC ₁₀ H ₇ - β (93)	106
	2-Phenylthio	<i>o</i> -C ₆ H ₄ SC ₆ H ₄ N=NC(NO ₂)=NNHC ₆ H ₄ SC ₆ H ₅ - <i>o</i>	20
	2-(<i>p</i> -Anisloxy)	N,N'-Di- <i>o</i> -(<i>p</i> -anisloxy)phenyl-C-nitroformazan†	20
	2-Phenoxy-4-phenyl	N,N'-Di-(2-phenoxy-4-phenyl)phenyl-C-nitroformazan†	20
	2-Phenylthio-4-phenyl	N,N'-Di-(2-phenylthio-4-phenyl)phenyl-C-nitroformazan†	20
Nitroethane	—	CH ₃ C(NO ₂)=NNHC ₆ H ₅ (quant.)	326, 1, 2, 107, 171, 324
	2-Methyl	CH ₃ C(NO ₂)=NNHC ₆ H ₄ CH ₃ - <i>o</i>	327
1-Nitropropane	4-Methyl	CH ₃ C(NO ₂)=NNHC ₆ H ₄ CH ₃ - <i>p</i>	324, 327
	4-Chloro	CH ₃ C(NO ₂)=NNHC ₆ H ₄ Cl- <i>p</i> (quant.)	176b
	4-Bromo	CH ₃ C(NO ₂)=NNHC ₆ H ₄ Br- <i>p</i>	328
	3-Nitro	CH ₃ C(NO ₂)=NNHC ₆ H ₄ NO ₂ - <i>m</i>	329
	4-Nitro	CH ₃ C(NO ₂)=NNHC ₆ H ₄ NO ₂ - <i>p</i>	324
	4-Sulfo	CH ₃ C(NO ₂)=NNHC ₆ H ₄ SO ₃ H- <i>p</i>	325
	2,4-Dichloro	CH ₃ C(NO ₂)=NNHC ₆ H ₃ Cl ₂ -2,4 (95)	330
	2,4,6-Trichloro	CH ₃ C(NO ₂)=NNHC ₆ H ₂ Cl ₃ -2,4,6†	330, 331
	2,4,6-Tribromo	CH ₃ C(NO ₂)=NNHC ₆ H ₂ Br ₃ -2,4,6 (49)†	331
	α -Naphthylamine	CH ₃ C(NO ₂)=NNHC ₁₀ H ₇ - α (5)	332
	β -Naphthylamine	CH ₃ C(NO ₂)=NNHC ₁₀ H ₇ - β	324, 332
	—	C ₂ H ₅ C(NO ₂)=NNHC ₆ H ₅ (87)	326, 4, 107, 324
1-Nitropropane	4-Methyl	C ₂ H ₅ C(NO ₂)=NNHC ₆ H ₄ CH ₃ - <i>p</i>	324
	4-Nitro	C ₂ H ₅ C(NO ₂)=NNHC ₆ H ₄ NO ₂ - <i>p</i>	324
	β -Naphthylamine	C ₂ H ₅ C(NO ₂)=NNHC ₁₀ H ₇ - β	324

4-Nitro-1-butanedisulfonic acid	4-Nitro	$p\text{-O}_2\text{NC}_4\text{H}_8\text{N}=\text{NC}(\text{NO}_2)(\text{C}_2\text{H}_5)_2\text{CH}_2\text{SO}_3\text{H}$ (51)	313
4 Phenylazo	4 Phenylazo	$p\text{-(C}_6\text{H}_5\text{N}=\text{N})\text{C}_4\text{H}_8\text{N}=\text{NC}(\text{NO}_2)(\text{C}_2\text{H}_5)_2\text{CH}_2\text{SO}_3\text{H}$ (56)	343
3,3'-Dimethoxybenzidine	3,3'-Dimethoxybenzidine	2,2'-(3,3'-Dimethoxy-4,4'-biphenyl)enediazobis[2-nitro-1-butanedisulfonic acid] (77)	343
2-Nitroethanol	—	$\text{HOCH}_2\text{C}(\text{NO}_2)=\text{NNHC}_2\text{H}_5$ (94)	107, 344
2-Nitropropanol	4 Sulfo	$\text{HOCH}_2\text{C}(\text{NO}_2)=\text{NNHC}_4\text{H}_8\text{SO}_3\text{H}\text{-}p$	344
1-Nitro-2-propanol	—	$\text{CH}_3\text{C}(\text{NO}_2)=\text{NNHC}_2\text{H}_5$ (78)	107
2-Nitro-1-butanol	—	$\text{CH}_3\text{CHOHC}(\text{NO}_2)=\text{NNHC}_2\text{H}_5$	107
—	—	$\text{C}_2\text{H}_5\text{C}(\text{NO}_2)=\text{NNHC}_2\text{H}_5$	107
4-Methyl	2-Methyl	$\text{HOCH}_2\text{C}(\text{NO}_2)(\text{C}_2\text{H}_5)\text{N}=\text{NC}_4\text{H}_8\text{CH}_3\text{-}p\ddagger$	108
2-Chloro	2-Chloro	$\text{HOCH}_2\text{C}(\text{NO}_2)(\text{C}_2\text{H}_5)\text{N}=\text{NC}_4\text{H}_8\text{Cl-o}\ddagger$	108
4-Chloro	4-Chloro	$\text{HOCH}_2\text{C}(\text{NO}_2)(\text{C}_2\text{H}_5)\text{N}=\text{NC}_4\text{H}_8\text{Cl-}p\ddagger$ (56)	108
—	—	$\text{C}_2\text{H}_5\text{C}(\text{NO}_2)=\text{NNHC}_4\text{H}_8\text{Cl-}p\parallel$	108
2-Bromo	2-Bromo	$\text{HOCH}_2\text{C}(\text{NO}_2)(\text{C}_2\text{H}_5)\text{N}=\text{NC}_4\text{H}_8\text{Br-o}\ddagger$	108
4-Bromo	4-Bromo	$\text{HOCH}_2\text{C}(\text{NO}_2)(\text{C}_2\text{H}_5)\text{N}=\text{NC}_4\text{H}_8\text{Br-}p\ddagger$	108
—	—	$\text{C}_2\text{H}_5\text{C}(\text{NO}_2)=\text{NNHC}_4\text{H}_8\text{Br-}p\parallel$	108
2,5-Dichloro	2,5-Dichloro	$\text{HOCH}_2\text{C}(\text{NO}_2)(\text{C}_2\text{H}_5)\text{N}=\text{NC}_4\text{H}_8\text{Cl}_2\text{-}2,5\ddagger$	108
2-Methyl-4-nitro	2-Methyl-4-nitro	$\text{C}_6\text{H}_5\text{C}(\text{NO}_2)=\text{NNHC}_4\text{H}_8\text{CH}_3\text{-}2\text{NO}_2\text{-}4$	108
5 Methyl-3-nitro	5 Methyl-3-nitro	$\text{HOCH}_2\text{C}(\text{NO}_2)(\text{C}_2\text{H}_5)\text{N}=\text{NC}_4\text{H}_8\text{CH}_3\text{-}5\text{-NO}_2\text{-}3\ddagger$	108
—	—	$\text{C}_2\text{H}_5\text{CHOHC}(\text{NO}_2)=\text{NNHC}_4\text{H}_8$	107
—	—	$\text{CH}_3\text{C}(\text{NO}_2)=\text{NNHC}_4\text{H}_8$	107
—	—	$\text{Cl}_3\text{CCHOHC}(\text{NO}_2)=\text{NNHC}_4\text{H}_8$	107

Note: References 177-480 are on pp. 136-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

‡ This product was obtained by acidification of the reaction mixture.

‖ This product was obtained when the alkaline reaction mixture was left for several days.

TABLE VII—Continued

COUPLING OF DIAZONIUM SALTS WITH NITRO COMPOUNDS

Nitro Compound	Substituent(s) in Aniline*	Product (Yield, %)	References
2-Nitro- <i>n</i> -butane	3-Nitro	$C_2H_5C(NO_2)(CH_3)N=NC_6H_4NO_2-m$	333
	4-Carboxy	$C_2H_5C(NO_2)(CH_3)N=NC_6H_4CO_2H-p$	333
2,5-Dichloro	2,5-Dichloro	$C_2H_5C(NO_2)(CH_3)N=NC_6H_3Cl_2-2,5$	333
2-Methyl-5-nitro	2-Methyl-5-nitro	$C_2H_5C(NO_2)(CH_3)N=NC_6H_4CH_3-2-NO_2-5$	333
2,4,6-Tribromo	2,4,6-Tribromo	$C_2H_5C(NO_2)(CH_3)N=NC_6H_2Br_3-2,4,6$	333
4-Phenylazo	4-Phenylazo	$C_2H_5C(NO_2)(CH_3)N=NC_6H_4(N=NC_6H_5)-p$	333
2-Methyl-1-nitropropane	—	$(CH_3)_2CHC(NO_2)=NNHC_6H_5$	5
	4-Sulfo	$(CH_3)_2CHC(NO_2)=NNHC_6H_4SO_3H-p$	325
1-Nitro- <i>n</i> -pentane	—	$n-C_4H_9C(NO_2)=NNHC_6H_5$ (90–100)	326
Dinitromethane	—	$C_6H_5N=NC(H)(NO_2)_2$	335
1,3-Dinitropropane	4-Nitro	$p-O_2NC_6H_4NHN=C(NO_2)_2$ (37)	19c
	—	$C_6H_5NHN=C(NO_2)CH_2C(NO_2)=NNHC_6H_5$	336
	4-Methyl	$p-CH_3C_6H_4NHN=C(NO_2)CH_2C(NO_2)=NNHC_6H_4CH_3-p$	336
	4-Methoxy	$p-CH_3OC_6H_4NHN=C(NO_2)CH_2C(NO_2)=NNHC_6H_4OCH_3-p$	336
1,5-Dinitro- <i>n</i> -pentane	—	$C_6H_5NHN=C(NO_2)(CH_3)_2C(NO_2)=NNHC_6H_5$	337
1,7-Dinitro- <i>n</i> -heptane	—	$C_6H_5NHN=C(NO_2)(CH_2)_5C(NO_2)=NNHC_6H_5$	338
Iodonitromethane	—	$IC(NO_2)=NNHC_6H_5$	339
	4-Methyl	$IC(NO_2)=NNHC_6H_4CH_3-p$	339
Methazonic acid	—	$C_6H_5NHN=C(NO_2)CH=NOH$	340
Nitroacetamide	4-Methyl	$p-CH_3C_6H_4NHN=C(NO_2)CH=NOH$	340
	—	$C_6H_5NHN=C(NO_2)CONH_2$	89
Methyl nitroacetate	4-Nitro	$p-O_2NC_6H_4NHN=C(NO_2)CONH_2$ (66)	19c
Ethyl nitroacetate	—	$C_6H_5NHN=C(NO_2)CO_2CH_3$ (56)	341
	—	$C_6H_5NHN=C(NO_2)CO_2C_2H_5$	342
	4-Nitro	$p-O_2NC_6H_4NHN=C(NO_2)CO_2C_2H_5$	342

4-Benzoyloxy	$C_6H_5C(NO_2)=NNHC_6H_4OCH_2C_6H_5$ (39)	171
3-Nitro	$C_6H_5C(NO_2)=NNHC_6H_4NO_2^m$ (quant.)	350
4-Nitro	$C_6H_5C(NO_2)=NNHC_6H_4NO_2^p$	111, 172, 350
4-Phenyl	$C_6H_5C(NO_2)=NNHC_6H_4C_6H_5$ (33)	171
2,4-Dinitro	$C_6H_5C(NO_2)=NNHC_6H_4(NO_2)_2$	350
2-Methyl-4-nitro	$C_6H_5C(NO_2)=NNHC_6H_4CH_3$ 2-NO ₂ -4	172
4-Methyl-2-nitro	$C_6H_5C(NO_2)=NNHC_6H_4CH_3$ 4-NO ₂ -2	172
2-Chloro-4-nitro	$C_6H_5C(NO_2)=NNHC_6H_4Cl$ 2-NO ₂ -4	172
β -Naphthylamine	$C_6H_5C(NO_2)=NNHC_{10}H_7$ (31)	171
2-(<i>o</i> -Nitrophenyl)	$C_6H_5C(NO_2)=NNHC_6H_4(C_6H_4NO_2-o)$ (55)	323a
4-Chloro-2-(4-chloro-2-nitro-phenyl)	$C_6H_5C(NO_2)=NNHC_6H_4Cl$ 4-(C ₆ H ₄ Cl-4-NO ₂ -2)-2 (35)	323a
4-Bromo-2-(4-bromo-2-nitro-phenyl)	$C_6H_5C(NO_2)=NNHC_6H_4Br$ 4-(C ₆ H ₄ Br-4-NO ₂ -2)-2	323a
α -Nitrobenzylcyanide	$C_6H_5C(CN)=NNHC_6H_4NO_2^p$	114
2-Methyl	$C_6H_5C(CN)=NNHC_6H_4CH_3$ 2-NO ₂ -4	114
4-Methyl	$C_6H_5C(CN)=NNHC_6H_4CH_3$ 4-NO ₂ -2	114
2-Chloro	$C_6H_5C(CN)=NNHC_6H_4Cl$ 2-NO ₂ -4	114
4-Chloro	$C_6H_5C(CN)=NNHC_6H_4Cl$ 4-NO ₂ -2	114
2-Nitro	$C_6H_5C(CN)=NNHC_6H_4(NO_2)_2$	114
4-Nitro	$C_6H_5C(CN)=NNHC_6H_4(NO_2)_2$	114
—	$p\text{-CH}_3OC_6H_4C(NO_2)=NNHC_6H_5$	114
<i>p</i> -Methoxy- α -nitrotoluene	$p\text{-CH}_3C_6H_4C(NO_2)=NNHC_6H_4(C_6H_4NO_2-o)$ (75)	351
<i>p</i> -Chloro- α -nitrotoluene	$m\text{-O}_2NC_6H_4C(NO_2)=NNHC_6H_5$ (quant.)	323a
α , <i>m</i> -Dinitrotoluene	$p\text{-O}_2NC_6H_4C(NO_2)=NNHC_6H_5$	352
α , <i>p</i> -Dinitrotoluene	$p\text{-O}_2NC_6H_4C(NO_2)=NNHC_6H_4NO_2^p$	352, 342

Note: References 177-480 are on pp. 136-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

TABLE VII—Continued
COUPLING OF DIAZONIUM SALTS WITH NITRO COMPOUNDS

Nitro Compound	Substituent(s) in Aniline*	Product (Yield, %)	References
1,1,1-Trichloro-3-nitro-2-propyl acetate	—	$\text{Cl}_3\text{CCH}(\text{O}_2\text{CCH}_3)\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_5$	345
	2-Methyl	$\text{Cl}_3\text{CCH}(\text{O}_2\text{CCH}_3)\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-o}$	345
	3-Methyl	$\text{Cl}_3\text{CCH}(\text{O}_2\text{CCH}_3)\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-m}$	345
	4-Methyl	$\text{Cl}_3\text{CCH}(\text{O}_2\text{CCH}_3)\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-p}$	345
	4-Chloro	$\text{Cl}_3\text{CCH}(\text{O}_2\text{CCH}_3)\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_3\text{Cl-p}$	345
	4-Nitro	$\text{Cl}_3\text{CCH}(\text{O}_2\text{CCH}_3)\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-p}$	345
2,4-Dichloro	—	$\text{Cl}_3\text{CCH}(\text{O}_2\text{CCH}_3)\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_3\text{Cl}_2\text{-2,4}$	345
	—	$\text{HOCH}_2\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_5$ (97)	107
2-Nitro-1,3-propanediol	—	$n\text{-C}_3\text{H}_7\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_5$	107
2-Nitro-1-pentanol	—	$n\text{-C}_5\text{H}_{11}\text{CHOHC}(\text{NO}_2)=\text{NNHC}_6\text{H}_5$	107
1-Nitro-2-pentanol	—	$n\text{-C}_4\text{H}_9\text{CHOHC}(\text{NO}_2)=\text{NNHC}_6\text{H}_5$	107
1-Nitro-2-hexanol	—	$\text{C}_6\text{H}_{13}\text{CHOHC}(\text{NO}_2)=\text{NNHC}_6\text{H}_5$	107
2-Nitro-1-phenylethanol	—	$\text{CH}_3\text{CHClCCl}_2\text{C}(\text{O}_2\text{CCH}_3)\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_5$	345
3,3,4-Trichloro-1-nitro-2-pentyl acetate	—	$\text{CH}_3\text{CHClCCl}_2\text{C}(\text{O}_2\text{CCH}_3)\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_5$	345
	4-Methyl	$\text{CH}_3\text{CHClCCl}_2\text{C}(\text{O}_2\text{CCH}_3)\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-p}$	345
	4-Chloro	$\text{CH}_3\text{CHClCCl}_2\text{C}(\text{O}_2\text{CCH}_3)\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_3\text{Cl-p}$	345
	4-Nitro	$\text{CH}_3\text{CHClCCl}_2\text{C}(\text{O}_2\text{CCH}_3)\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-p}$	345
	4-Nitro	$p\text{-O}_2\text{NC}_6\text{H}_4\text{N}=\text{NC}(\text{NO}_2)=\text{NNHC}_6\text{H}_4\text{NO}_2\text{-p}$	340
	—	$\text{C}_6\text{H}_5\text{CHOHC}(\text{NO}_2)\text{CH}(\text{C}_6\text{H}_5)\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_5$	347
1-Benzoyl-2-nitroethanol	—	$\text{C}_6\text{H}_5\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_5$ (80)	171, 318, 319
2,4-Dinitro-1,3-diphenyl-1-butanol	—	$\text{C}_6\text{H}_5\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-p}$ (40)	171
α -Nitrotoluene	4-Methyl	$\text{C}_6\text{H}_5\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_4\text{CH}_3\text{-p}$ (40)	171
	4-Methoxy	$\text{C}_6\text{H}_5\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_4\text{OCH}_3\text{-p}$ (33)	171
	4-Butoxy	$\text{C}_6\text{H}_5\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_4\text{OC}_4\text{H}_9\text{-p}$ (34)	171

2-Methyl-4-nitro	$C_6H_4CON=NC_6H_4CH_3-2-NO_2-4$	110
4-Methyl-2-nitro	$C_6H_4CON=NC_6H_4CH_3-4-NO_2-2$	110
4-Methyl-3-nitro	$C_6H_4CON=NC_6H_4CH_3-4-NO_2-3$	110
2,4,6-Tribromo	$C_6H_3CON=NC_6H_3Br_3-2,4,6$	110
—	$p-CH_3C_6H_4C(NO_2)=NNHC_6H_4NO_2-p$	109, 358
—	$p-CH_3OC_6H_4C(NO_2)=NNHC_6H_4NO_2-p$	109, 358
—	4-(2-Nitro-2-phenylazopropyl)morpholine (22)	176a
4-Chloro	4-[(2-Nitro-2-(<i>p</i> -chlorophenylazo)propyl)morpholine (26)]	176a
2-Nitro	4-[(2-Nitro-2-(<i>o</i> -nitrophenylazo)propyl)morpholine (32)]	176a
3-Nitro	4-[(2-Nitro-2-(<i>m</i> -nitrophenylazo)propyl)morpholine (41)]	176a
4-Nitro	4-[(2-Nitro-2-(<i>p</i> -nitrophenylazo)propyl)morpholine (46)]	176a
2 Carboxy	4-[(2-Nitro-2-(<i>o</i> -carboxyphenylazo)propyl)morpholine (13)]	176a
4-Carboxy	4-[(2-Nitro-2-(<i>p</i> -carboxyphenylazo)propyl)morpholine (26)]	176a
2,4-Dichloro	4-[(2-Nitro-2-(2,4-dichlorophenylazo)propyl)morpholine (18)]	176a
β -Naphthylamine	4-[(2-Nitro-2- β -naphthylazo)propyl)morpholine (25)]	176a
4-Phenylazo	4-[(2-Nitro-2-(<i>p</i> -phenylazophenylazo)propyl)morpholine (80)]	176a
4-Chloro	2-(<i>p</i> -chlorophenylazo)-2-nitrotributylamine (7)	176a
1-Di- <i>n</i> -butylamino-2-nitro-butane	2- β -Naphthylazo-2-nitrotributylamine (17)	176a
2,3-Diphenyl-1,4-dinitrobutane	2,3-Diphenyl-1,4-dihydrazono-1,4-dinitrobutane (89)	359
2,3-Di-(3,4-methylenedioxyphenyl)-1,4-dinitrobutane	2,3-Di-(3,4-methylenedioxyphenyl)-1,4-dihydrazono-1,4-dinitrobutane	359
Nitromethyl <i>p</i> -tolyl sulfoxide	$p-CH_3C_6H_4S(OC_6H_4NO_2)=NNHC_6H_4NO_2-p$ (43)	19c

Note: References 177-480 are on pp. 130-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

TABLE VII—Continued

COUPLING OF DIAZONIUM SALTS WITH NITRO COMPOUNDS

Nitro Compound	Substituent(s) in Aniline*	Product (Yield, %)	References
α -Nitroacetophenone	—	$C_6H_5COC(NO_2) = NNHC_6H_5$ (60)	353
	1-Chloro	$C_6H_5COC(NO_2) = NNHC_6H_4Cl-p$	353
	4-Bromo	$C_6H_5COC(NO_2) = NNHC_6H_4Br-p$	353
	2-Nitro	$C_6H_5COC(NO_2) = NNHC_6H_3NO_2-o$	353
	4-Nitro	$C_6H_5COC(NO_2) = NNHC_6H_4NO_2-p$	312, 353
	2,4-Dichloro	$C_6H_5COC(NO_2) = NNHC_6H_3Cl_2-2,4$	353
	2,5-Dichloro	$C_6H_5COC(NO_2) = NNHC_6H_3Cl_2-2,5$	353
	2,4-Dibromo	$C_6H_5COC(NO_2) = NNHC_6H_3Br_2-2,4$	353
	2,4,6-Tribromo	$C_6H_5COC(NO_2) = NNHC_6H_2Br_3-2,4,6$	353
	2,4,5-Tribromo	$C_6H_5COC(NO_2) = NNHC_6H_2Br_3-2,4,5$	353
1-Nitro-3-phenylpropane	—	$C_6H_5(CH_2)_3C(NO_2) = NNHC_6H_5$	351
Diphenyltrimethane	—	$(C_6H_5)_3C = NNHC_6H_4NO_2-p$	112, 113
α,α -Dimethyltoluene	2-Methyl	$C_6H_5C(NO_2) = NNHC_6H_4NO_2-p$	109, 111, 355
	4-Methyl	$C_6H_5C(NO_2) = NNHC_6H_3CH_3-2-NO_2-4$	109, 356
	2-Chloro	$C_6H_5CON = NC_6H_4CH_3-p$	356
	4-Chloro	$C_6H_5C(NO_2) = NNHC_6H_3Cl-2-NO_2-4$	109, 356
	2-Bromo	$C_6H_5CON = NC_6H_4Cl-p$	356
	4-Bromo	$C_6H_5C(NO_2) = NNHC_6H_3Br-2-NO_2-4$	109, 356
	2,4-Dimethyl	$C_6H_5CON = NC_6H_3(CH_3)_2-2,4$	350, 357

Indene	2,4-Dinitro	3-(2,4-Dinitrophenylazo)-2,5-dimethyl-2,4-hexadiene	116
<i>p</i> -Methoxystyrene	2,4-Dinitro	1-(2,4-Dinitrophenylazo)indene	118
Phenylacetylene	2,4-Dinitro	<i>p</i> -CH ₃ OC ₆ H ₄ CH=NNHC ₆ H ₄ (NO ₂) ₂ -2,4 (21)	124
<i>p</i> -Methoxyphenylacetylene	4-Nitro	C ₆ H ₅ COCH=NNHC ₆ H ₄ NO ₂ - <i>p</i> (13)	124
	4-Nitro	<i>p</i> -CH ₃ OC ₆ H ₄ COCH=NNHC ₆ H ₄ NO ₂ - <i>p</i> (33)	124
Anethole	2,4-Dinitro	<i>p</i> -CH ₃ OC ₆ H ₄ COCH=NNHC ₆ H ₄ (NO ₂) ₂ -2,4 (69)	124
	4-Nitro	<i>p</i> -CH ₃ OC ₆ H ₄ CH=NNHC ₆ H ₄ NO ₂ - <i>p</i> (71)†	127
<i>o</i> -Propenylphenol	2,4-Dinitro	<i>p</i> -CH ₃ OC ₆ H ₄ CH=NNHC ₆ H ₄ (NO ₂) ₂ -2,4 (62)†	127
<i>p</i> -Propenylphenol	4-Nitro	<i>o</i> -HOC ₆ H ₄ CH=NNHC ₆ H ₄ NO ₂ - <i>p</i> (25)†	130
Isosafrole	4-Nitro	<i>p</i> -HOC ₆ H ₄ CH=NNHC ₆ H ₄ NO ₂ - <i>p</i> (66)†	130
	4-Nitro	Piperonal <i>p</i> -nitrophenylhydrazones (72)†	127
Isoeugenol	2,4-Dinitro	Piperonal 2,4-dinitrophenylhydrazones†	127
	4-Nitro	Vaillin <i>p</i> -nitrophenylhydrazones (86)†	128
Isoapiole	2,4-Dinitro	Vaillin 2,4-dinitrophenylhydrazones†	128
<i>p</i> -Propenyldimethylamine	4-Nitro	Aptolaldehyde <i>p</i> -nitrophenylhydrazones†	127
1,1-Diphenylethylene	4-Nitro	<i>p</i> -(CH ₃) ₂ NC ₆ H ₄ CH=NNHC ₆ H ₄ NO ₂ - <i>p</i> ††	129
1,1-Bis-(<i>p</i> -tolyl)ethylene	2,4-Dinitro	(C ₆ H ₅) ₂ C=CHN=NC ₆ H ₄ (NO ₂) ₂ -2,4	14
	4-(<i>p</i> -Phenyl-mercaptobenzoyl)	(<i>p</i> -CH ₃ C ₆ H ₄) ₂ C=CHN=NC ₆ H ₄ (COC ₆ H ₄ SC ₆ H ₄ - <i>p</i>)- <i>p</i>	13
1,1-Bis-(<i>p</i> -anisyl)ethylene	4-Nitro	(<i>p</i> -CH ₃ OC ₆ H ₄) ₂ C=CHN=NC ₆ H ₄ NO ₂ - <i>p</i> (40)	14
	4-(<i>p</i> -Phenyl-mercaptobenzoyl)	(<i>p</i> -CH ₃ OC ₆ H ₄) ₂ C=CHN=NC ₆ H ₄ (COC ₆ H ₄ SC ₆ H ₄ - <i>p</i>)- <i>p</i>	13
1-Phenyl-1-(<i>p</i> -anisyl)ethylene	—	<i>p</i> -CH ₃ OC ₆ H ₄ C(C ₆ H ₅)=CHN=NC ₆ H ₄	14
	2,4-Dinitro	<i>p</i> -CH ₃ OC ₆ H ₄ C(C ₆ H ₅)=CHN=NC ₆ H ₄ (NO ₂) ₂ -2,4 (40)	14

Note. References 177-180 are on pp. 138-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

† These products were obtained by the addition of the dry diazonium salt to an ethanolic solution of the reactant.
‡ When an alcoholic solution of the reactant was added to the dry diazonium salt, the entire side chain was eliminated to give a nearly quantitative yield of *N,N*-dimethyl-*p*-(*p*-nitrophenylazo)aniline.¹⁴⁴

TABLE VIII

COUPLING OF DIAZONIUM SALTS WITH HYDROCARBONS

A. *Unsaturated Hydrocarbons*

Hydrocarbon	Substituent(s) in Aniline*	Product (Yield, %)	References
2-Methylpropene	4-Amino	$(CH_3)_2C=CHN=NC_6H_4N=NC(CH_3)_2$	116
1,3-Butadiene	2,4-Dinitro	$2,4-(O_2N)_2C_6H_3N=NCCH=CHCH=CH_2$	116
	4-Nitro	$p-O_2NC_6H_4N=NCCH=CHCH=CH_2$	360
	2,4-Dinitro	$2,4-(O_2N)_2C_6H_3N=NCCH=CHCH=CH_2$ (13)	115
2-Methyl-2-butene	4-Amino	$(CH_3)_2C=C(CH_3)N=NC_6H_4N=NC(CH_3)_2$	116
	2,4-Dinitro	$2,4-(O_2N)_2C_6H_3N=NC(CH_3)_2$	116
1,3-Pentadiene	4-Amino	$CH_2=CHCH=CHCH=CH_2$	110
		$NC(CH_3)_2=CHCH=CH_2$	
	4-Nitro	$p-O_2NC_6H_4N=NC(CH_3)_2=CHCH=CH_2$	115, 116
	2,4-Dinitro	$2,4-(O_2N)_2C_6H_3N=NC(CH_3)_2=CHCH=CH_2$	115, 116
2-Methyl-1,3-butadiene	4-Nitro	$p-O_2NC_6H_4N=NCCH=C(CH_3)CH=CH_2$	361a
	2,4-Dinitro	$2,4-(O_2N)_2C_6H_3N=NC(CH_3)_2=CHCH=CH_2$	115
2,4-Hexadiene	4-Nitro	$p-O_2NC_6H_4N=NC(CH_3)_2=CHCH=CHCH_3$	116, 360
	2,4-Dinitro	$2,4-(O_2N)_2C_6H_3N=NC(CH_3)_2=CHCH=CHCH_3$	116
2-Methyl-2,4-pentadiene	2,4-Dinitro	$2,4-(O_2N)_2C_6H_3N=NCCH=CHCH=C(CH_3)_2$ (49)	361b
2,3-Dimethyl-1,3-butadiene	4-Nitro	$p-O_2NC_6H_4N=NCCH=C(CH_3)C(CH_3)=CH_2$ (47)	115
	2,4-Dinitro	$2,4-(O_2N)_2C_6H_3N=NCCH=C(CH_3)C(CH_3)=CH_2$	115
Cyclopentadiene	—	1-Phenylazocyclopentadiene (small)	117, 362
	4-Nitro	1-(<i>p</i> -Nitrophenylazo)cyclopentadiene	118
	2,4-Dinitro	1-(2,4-Dinitrophenylazo)cyclopentadiene	118
2,4-Cyclopentadiene-1-carboxylic acid	2-Hydroxy-5-sulfo	1-(2-Hydroxy-5-sulfophenylazo)-2,4-cyclopentadiene-1-carboxylic acid (40)	363
2,5-Dimethyl-2,4-hexadiene	4-Amino	3,3'-(<i>p</i> -Phenylenedisazo)bis-(2,5-dimethyl-2,4-hexadiene)	116
	4-Nitro	3-(<i>p</i> -Nitrophenylazo)-2,5-dimethyl-2,4-hexadiene	116

N-Methylquinaldinium methosulfate	4-Nitro	1,2-Dihydro-1-methyl-2-(<i>p</i> -nitrophenylazomethylene)- quinoline	132 <i>g</i>
	2,5-Dichloro	1,2-Dihydro-1-methyl-2-(2,5-dichlorophenylazomethylene)- quinoline	132 <i>g</i>
	2-Methoxy-5-chloro	1,2-Dihydro-1-methyl-2-(2-methoxy-5-chlorophenylazo- methylene)quinoline	132 <i>g</i>
	2-Methoxy-4-nitro	1,2-Dihydro-1-methyl-2-(2-methoxy-4-nitrophenylazo- methylene)quinoline	132 <i>g</i>
N-Ethylepidinium iodide	4-Nitro	1,4-Dihydro-1-ethyl-4-(<i>p</i> -nitrophenylazomethylene)- quinoline	132 <i>g</i>
	2,5-Dichloro	1,4-Dihydro-1-ethyl-4-(2,5-dichlorophenylazomethylene)- quinoline	132 <i>g</i>
	2-Methoxy-5-chloro	1,4-Dihydro-1-ethyl-4-(2-methoxy-5-chlorophenylazo- methylene)quinoline	132 <i>g</i>
	2-Methoxy-4-nitro	1,4-Dihydro-1-ethyl-4-(2-methoxy-4-nitrophenylazo- methylene)quinoline	132 <i>g</i>
2,3,3-Trimethylindolenine	—	3,3-Dimethylindolenine-2-carboxaldehyde phenyl- hydrazone (60-90)	132 <i>a</i>
	4-Chloro	3,3-Dimethylindolenine-2-carboxaldehyde <i>p</i> -chloro- phenylhydrazone (90-99)	132 <i>a</i>
	4-Nitro	3,3-Dimethylindolenine-2-carboxaldehyde <i>p</i> -nitrophenyl- hydrazone	132 <i>a</i>
1,2,3,3-Tetramethylindolenium iodide	—	1,2-Dihydro 2-phenylazomethylene-1,3,3-trimethylindoline	133, 135
	4-Nitro	1,2-Dihydro-2-(<i>p</i> -nitrophenylazomethylene)-1,3,3- trimethylindoline	133, 135
	4-Iodo	1,2-Dihydro-2-(<i>p</i> -iodophenylazomethylene)-1,3,3- trimethylindoline	133
	2-Methoxy-4-nitro	1,2-Dihydro 2-(2-methoxy-4-nitrophenylazomethylene)- 1,3,3 trimethylindoline	135

Note: References 177-480 are on pp 130-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

TABLE VIII—Continued

A. Unsaturated Hydrocarbons—Continued

Hydrocarbon	Substituent(s) in Aniline*	Product (Yield, %)	References
1,1-Bis-(<i>p</i> -dimethylamino-phenyl)ethylene	—	$[p-(CH_3)_2NC_6H_4]_2C=CHN=NC_6H_5$	14
	4-Nitro	$[p-(CH_3)_2NC_6H_4]_2C=CHN=NC_6H_4NO_2-p$	14
	2,4-Dinitro	$[p-(CH_3)_2NC_6H_4]_2C=CHN=NC_6H_3(NO_2)_3-2,4$	14
1-Aminoanthraquinone	—	$[p-(CH_3)_2NC_6H_4]_2C=CHN=NC_{14}H_7O_2$ (SS)	14
1-Phenyl-1-(<i>p</i> -dimethylamino-phenyl)ethylene	—	$p-(CH_3)_2NC_6H_4C(C_6H_5)=CHN=NC_6H_5$	14
	4-Nitro	$p-(CH_3)_2NC_6H_4C(C_6H_5)=CHN=NC_6H_4NO_2-p$	14
	2,4-Dinitro	$p-(CH_3)_2NC_6H_4C(C_6H_5)=CHN=NC_6H_3(NO_2)_3-2,4$	14
1-Phenyl-1,3-butadiene	4-Nitro	$C_6H_5CH=CHCH=CHN=NC_6H_4NO_2-p$	365
2,3-Diphenyl-1,3-butadiene	2,4-Dinitro	$2,4-(O_2N)_2C_6H_3N=NCH=C(C_6H_5)C(C_6H_5)=CH_2$	366

B. Compounds Containing a Reactive Methyl Group

Reactive Methyl Compound	Substituent(s) in Aniline	Product (Yield, %)	References
α -Picoline	4-Nitro	α -Picolinaldehyde <i>p</i> -nitrophenylhydrazone (58)	132
2,4,6-Trinitrotoluene	4-Nitro	2,4,6-Trinitrobenzaldehyde <i>p</i> -nitrophenylhydrazone (86)	132
2-Methylimidazole	4-Nitro	Imidazole-2-carboxaldehyde <i>p</i> -nitrophenylhydrazone (64)	132
2,6-Dimethyl-3,5-dicarboxypyridine	4-Nitro	3,5-Dicarboxy-6-methylpyridine-2-carboxaldehyde <i>p</i> -nitrophenylhydrazone (94)	132
N-Methylquinazolinum iodide	—	1,2-Dihydro-1-methyl-2-phenylazomethylenequinoline	133, 134
	4-Nitro	1,2-Dihydro-1-methyl-2-(<i>p</i> -nitrophenylazomethylene)-quinoline	133, 134

TABLE VIII—Continued
B. Compounds Containing a Reactive Methyl Group—Continued

Reactive Methyl Compound	Substituent(s) in Aniline	Product (Yield, %)	References
2-Methylbenzothiazole	4-Nitro	Benzothiazole-2-carboxaldehyde <i>p</i> -nitrophenylhydrazone (30)	368a, b
2,3-Dimethylbenzothiazolium iodide	—	2-[Bis(phenylazo)methylene]-3-methylbenzothiazoline	132c
	4-Nitro	2-[Bis-(<i>p</i> -nitrophenylazo)methylene]-3-methylbenzo- thiazoline	132c
2,3-Dimethylbenzothiazolium methosulfate	—	2-[Bis-(phenylazo)methylene]-3-methylbenzothiazoline (80)	132d
	4-Methyl	2-[Bis-(<i>p</i> -tolylazo)methylene]-3-methylbenzothiazoline	132d
	4-Methoxy	2-[Bis-(<i>p</i> -anisylazo)methylene]-3-methylbenzothiazoline	132d
	4-Chloro	2-[Bis-(<i>p</i> -chlorophenylazo)methylene]-3-methylbenzo- thiazoline	132b, 132d
	2-Nitro	2-[Bis-(<i>o</i> -nitrophenylazo)methylene]-3-methylbenzo- thiazoline	132d
	4-Nitro	2-(<i>p</i> -Nitrophenylazomethylene)-3-methylbenzothiazoline	132g
		2-[Bis-(<i>p</i> -nitrophenylazo)methylene]-3-methylbenzo- thiazoline	132b, 132d
	4-Sulfo	2-[Bis-(<i>p</i> -sulfophenylazo)methylene]-3-methylbenzo- thiazoline	132d
	2,5-Dichloro	2-[Bis-(2,5-dichlorophenylazo)methylene]-3-methylbenzo- thiazoline	132d
	2-Methoxy-4-nitro	2-(2-Methoxy-4-nitrophenylazomethylene)-3-methylbenzo- thiazoline	132g
	4-Chloro	2-[Bis-(<i>p</i> -chlorophenylazo)methylene]-3-ethylbenzo- thiazoline	132b
2-Methyl-3-ethylbenzo- thiazolium iodide	4-Nitro	2-[Bis-(<i>p</i> -nitrophenylazo)methylene]-3-ethylbenzo- thiazoline	132b, 132c

2,5-Dichloro	9,10-Dihydro-9-methyl-10-(2,5-dichlorophenylazo-methylene)acridine	132g
2,4-Dinitro	9,10-Dihydro-9-methyl-10-(2,4-dinitrophenylazo-methylene)acridine	14
2-Methoxy-5-chloro	9,10-Dihydro 9-methyl-10-(2-methoxy-5-chlorophenylazo-methylene)acridine	132g
2-Methoxy-4 nitro	9,10-Dihydro-9-methyl-10 (2-methoxy 4-nitrophenylazo-methylene)acridine	132g
2-Acetamido 9 methylacridine	2-Acetamidooacridine-9-carboxaldehyde phenylhydrazones (66)	132
4-Nitro	2-Acetamidooacridine-9-carboxaldehyde <i>p</i> nitrophenylhydrazones (55)	132
—	Xanthene-9-carboxaldehyde phenylhydrazones	14
4-Nitro	Xanthene-9-carboxaldehyde <i>p</i> -nitrophenylhydrazones	14
2,4-Dinitro	Xanthene 9-carboxaldehyde 2,4-dinitrophenylhydrazones	14
—	Thioxanthene 9-carboxaldehyde phenylhydrazones	14
4-Nitro	Thioxanthene-9-carboxaldehyde <i>p</i> -nitrophenylhydrazones	14
2,4 Dinitro	Thioxanthene-9-carboxaldehyde 2,4 dinitrophenylhydrazones	14
—	1-Phenyl-3-methyl-4- α -(phenylazomethyl)ethylidene-2-pyrazolin-5-one (57)	135a
4-Nitro	1-Phenyl 3-methyl-4- α (p-nitrophenylazomethyl)-ethylidene 2-pyrazolin-5-one (76)	135a
3-Carboxy	1-Phenyl-3-methyl-4- α -(<i>m</i> -carboxyphenylazomethyl)-ethylidene-2-pyrazolin-5-one (82)	135a
2,5-Dichloro	1-Phenyl 3-methyl-4 α -(2,5-dichlorophenylazomethyl)-ethylidene-2-pyrazolin-5-one (51)	135a

TABLE VIII—Continued
B. Compounds Containing a Reactive Methyl Group—Continued

Reactive Methyl Compound	Substituent(s) in Aniline	Product (Yield, %)	References
9-Methylacridine	—	Acridine-9-carboxaldehyde phenylhydrazine	131
	2-Methyl	Acridine-9-carboxaldehyde <i>o</i> -tolylhydrazine	131
	3-Methyl	Acridine-9-carboxaldehyde <i>m</i> -tolylhydrazine	131
	4-Methyl	Acridine-9-carboxaldehyde <i>p</i> -tolylhydrazine	131
	2-Methoxy	Acridine-9-carboxaldehyde <i>o</i> -anisylhydrazine	131
	4-Methoxy	Acridine-9-carboxaldehyde <i>p</i> -anisylhydrazine	131
	4-Hydroxy	Acridine-9-carboxaldehyde <i>p</i> -hydroxyphenylhydrazine	131
	4-Chloro	Acridine-9-carboxaldehyde <i>p</i> -chlorophenylhydrazine	131
	4-Iodo	Acridine-9-carboxaldehyde <i>p</i> -iodophenylhydrazine	131
	2-Nitro	Acridine-9-carboxaldehyde <i>o</i> -nitrophenylhydrazine	131
	3-Nitro	Acridine-9-carboxaldehyde <i>m</i> -nitrophenylhydrazine	131
	4-Nitro	Acridine-9-carboxaldehyde <i>p</i> -nitrophenylhydrazine	131
	2-Carboxy	Acridine-9-carboxaldehyde <i>o</i> -carboxyphenylhydrazine	131
	3-Carboxy	Acridine-9-carboxaldehyde <i>m</i> -carboxyphenylhydrazine	131
	4-Carboxy	Acridine-9-carboxaldehyde <i>p</i> -carboxyphenylhydrazine	131
	4-Sulfo	Acridine-9-carboxaldehyde <i>p</i> -sulfoxyphenylhydrazine	131
	2,4-Dimethyl	Acridine-9-carboxaldehyde 2,4-dimethylphenylhydrazine	131
	2,4-Dinitro	Acridine-9-carboxaldehyde 2,4-dinitrophenylhydrazine	131
	2,5-Dimethoxy-4-phenylamino	Acridine-9-carboxaldehyde 2,5-dimethoxy-4-(phenylamino)phenylhydrazine (43)	132
9,10-Dimethylacridinium methosulfate	—	9,10-Dihydro-9-methyl-10-phenylazomethyleneacridine	14
	4-Nitro	9,10-Dihydro-9-methyl-10-(<i>p</i> -nitrophenylazomethylene)-acridine	14, 132 ^g

TABLE VIII—Continued

B. Compounds Containing a Reactive Methyl Group—Continued

Reactive Methyl Compound	Substituent(s) in Aniline	Product (Yield, %)	References
1-Phenyl-3-methyl-4- α -methyl- benzylidene-2-pyrazolin-5-one	—	1-Phenyl-3-methyl-4- α -phenylazomethylbenzylidene-2- pyrazolin-5-one (70)	135a
	4-Nitro	1-Phenyl-3-methyl-4- α -(<i>p</i> -nitrophenylazomethyl)benzyl- idene-2-pyrazolin-5-one (73)	135a
	2-Carboxy	1-Phenyl-3-methyl-4- α -(<i>o</i> -carboxyphenylazomethyl)- benzylidene-2-pyrazolin-5-one (82)	135a
	2,5-Dichloro	1-Phenyl-3-methyl-4- α -(2,5-dichlorophenylazomethyl)- benzylidene-2-pyrazolin-5-one (87)	135a
	4-Chloro-2-nitro	1-Phenyl-3-methyl-4- α -(4-chloro-2-nitrophenylazomethyl)- benzylidene-2-pyrazolin-5-one (47)	135a
1-Phenyl-3-methyl-4-(α -methyl- <i>m</i> -nitrobenzylidene)-2- pyrazolin-5-one	4-Nitro	1-Phenyl-3-methyl-4- α -(<i>p</i> -nitrophenylazomethyl)- <i>m</i> - nitrobenzylidene-2-pyrazolin-5-one (52)	135a

C. Cinnolines from *o*-Aminophenylethylenes

Substituent(s) in Cinnoline (Yield, %)



Amine

o-Amino- α -methylstyrene
 2-(2'-Amino-5'-chlorophenyl)propene
 2-(2'-Amino-4'-chlorophenyl)propene

References

368, 369
 369
 369

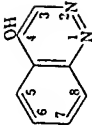
E. *Indazoles from o-Toluidine*Product, Substituent(s)
in Indazole

Reactant, Substituent(s) in Aniline	(Yield, %)	References
2-Methyl	— (3-5)	130, 138
2-Cyanoethyl	3-Cyano (71)	95b, 168
2-Methyl-7-nitro	4-Nitro (90-98)	137, 376
2,4-Dimethyl	5-Methyl	130
2-Methyl-4-nitro	5-Nitro (82-90)	137, 138, 370
2-Methyl-5-nitro	6-Nitro (90-96)	137, 374, 375, 376
2-Methyl-6-nitro	7-Nitro (80)	137, 376
2,4,6-Trimethyl	5,7-Dimethyl (small)	130
2,4-Dinitro-6-methyl	5,7-Dinitro (31-38)	378
2,3-Trimethyl-4-nitro	4-Methyl-5-nitro (70-86)	137
2,3-Trimethyl-5-nitro	4-Methyl-6-nitro (91)	137
2,3-Trimethyl-6-nitro	4-Methyl-7-nitro (100)	137
2,4-Dimethyl-3-nitro	5-Methyl-4-nitro (79)	137
2,4-Dimethyl-5-nitro	5-Methyl-6-nitro (75-80)	137
2,4-Dimethyl-6-nitro	5-Methyl-7-nitro (48-53)	137
2,5-Trimethyl-3-nitro	6-Methyl-4-nitro (93)	137, 377
2,5-Dimethyl-4-nitro	6-Methyl-5-nitro (83)	137

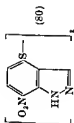
Note. References 177-180 are on pp. 130-142.

* This is an over-all yield from the nitro compound.

TABLE VIII—Continued
D. 4-Hydroxycinnolines from o-Aminophenylacetylenes

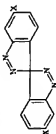
Amine	Substituent(s) in	(Yield, %)	References
<i>o</i> -Aminophenylacetylene		—	125
2-Amino-5-methoxyphenylacetylene	6-Methoxy	60	125
2-Amino-5-chlorophenylacetylene	6-Chloro (20*)	23	23
2-Amino-5-bromophenylacetylene	6-Bromo (20*)	23	23
1-(<i>o</i> -Aminophenyl)-2-phenylacetylene	3-Phenyl (55)	23	23
1-(2'-Amino-4'-methoxyphenyl)-2-phenylacetylene	6-Methoxy-3-phenyl	23	23
<i>o</i> -Aminophenylpropionic acid	3-Carboxy (60)	367, 125, 126	23
2-Amino-5-chlorophenylpropionic acid	3-Carboxy-6-chloro (66)	23	23
2-Amino-5-bromophenylpropionic acid	3-Carboxy-6-bromo (66)	23	23
2-Amino-5-methoxyphenylpropionic acid	3-Carboxy-6-methoxy (68*)	125	125
2-Amino-4,5-methylenedioxyphenylpropionic acid	3-Carboxy-6,7-methylenedioxy (37*)	125	125

Reactant



380

Substituents X in



Bis-(2-amino-4-chlorophenyl)methane
 Bis-(2-amino-4-cyanophenyl)methane
 Bis-(2-amino-4-acetylphenyl)methane
 Bis-(2-amino-4-acetamidophenyl)methane
 Bis-(2-amino-4-carboxyphenyl)methane
 Bis-(2-amino-4-carbethoxyphenyl)methane

Chloro

Cyano

Acetyl

Acetamido

Carboxy

Carbethoxy

384

385

385

385

385

386

Note: References 177-480 are on pp 138-142.

* One nitro group was replaced by chlorine when the diazotization was run in hydrochloric acid.

† This product was prepared by tetrazotizing the amine and reacting the tetrazonium salt with sodium azide.

TABLE VIII—Continued
E. Indazoles from o-Toluidines—Continued

Reactant, Substituent(s) in Aniline	Product, Substituent(s) in Indazole	Yield, %	References
2,5-Dimethyl-6-nitro	6-Methyl-7-nitro (81)	137	137
2,6-Dimethyl-3-nitro	7-Methyl-4-(or 6-)nitro (100)	137	137
3-Chloro-2-methyl-4-nitro	4-Chloro-5-nitro (86)	380	380
3-Chloro-2-methyl-6-nitro	4-Chloro-7-nitro	379	379
4-Chloro-2-methyl-6-nitro	5-Chloro-7-nitro	379	379
2,3-Dinitro-6-methyl	7-Chloro-6-nitro* (85)	380	380
3-Methoxy-2-methyl-6-nitro	4-Methoxy-7-nitro	379	379
3-Methoxy-6-methyl-2-nitro	6-Methoxy-7-nitro (83)	383	383
3-Diethylsulfamyl-2-methyl-6-nitro	4-Diethylsulfamyl-7-nitro	379	379
2,4,5-Trimethyl-3-nitro	5,6-Dimethyl-4-(or 6-)nitro (100)	137	137
3,4,6-Trimethyl-2-nitro	5,6-Dimethyl-7-nitro (20)	137	137
2,4,6-Trimethyl-3-nitro	5,7-Dimethyl-4-(or 6-)nitro (80)	137	137
2,4-Dimethyl-3,5-dinitro	7-Methyl-4,6-dinitro (86)	137	137
2,6-Dimethyl-3,5-dinitro	6-Methyl-5,7-dinitro (100)	137	137
3,6-Dimethyl-2,4-dinitro	5,7-Dinitro-6-sulfo	381	381
2,4-Dinitro-6-methyl-3-sulfo	5,7-Dimethyl-4-triazo†	382	382
2,4,6-Trimethyl-3-amino	5,6-Dimethyl-4,7-dinitro (75-85)	137	137
2,5-Dinitro-3,4,6-trimethyl	5,7-Dimethyl-4,6-dinitro (100)	137	137
3,5-Dinitro-2,4,6-trimethyl			



CH ₃	2,4-(O ₂ N) ₂ C ₆ H ₃	p-O ₂ NC ₆ H ₄	390
CH ₃	(C ₆ H ₅) ₂ NCO	C ₆ H ₅	398d
CH ₃ O ₂ C	C ₆ H ₅	C ₆ H ₅	143
CH ₃ O ₂ C	C ₆ H ₅	p-O ₂ NC ₆ H ₄	143
CH ₃ O ₂ C	2,4-(CH ₃) ₂ C ₆ H ₃ *	C ₆ H ₅	143
CH ₃ O ₂ C	2,4-(CH ₃) ₂ C ₆ H ₃ *	p-BrC ₆ H ₄	143
CH ₃ O ₂ C	2,4-(CH ₃) ₂ C ₆ H ₃ *	p-O ₂ NC ₆ H ₄	143
C ₂ H ₅ O ₂ C	C ₆ H ₅	C ₆ H ₅	148
C ₂ H ₅ O ₂ C	p-HO ₂ SC ₆ H ₄ †	C ₆ H ₅	401
C ₂ H ₅	C ₆ H ₅	C ₆ H ₅	393, 392
CH ₃ CO	C ₆ H ₅	C ₆ H ₅	52, 226
CH ₃ CO	C ₆ H ₅	C ₆ H ₅	52
CH ₃ CO	C ₆ H ₅	p-CH ₃ C ₆ H ₄	52
n-C ₃ H ₇	C ₆ H ₅	p-O ₂ NC ₆ H ₄	389
n-C ₃ H ₇	C ₆ H ₅	p-HO ₂ SC ₆ H ₄	392
n-C ₃ H ₇	Cholyl (C ₂₄ H ₄₈ O ₆)	C ₆ H ₅	387
CH ₂ =C(CH ₃)	C ₆ H ₅	C ₆ H ₅	393a
(CH ₃) ₂ CHCH ₂	C ₆ H ₅	C ₆ H ₅	392
n-C ₃ H ₇	C ₆ H ₅	C ₆ H ₅	81
n-C ₃ H ₇	C ₆ H ₅	C ₆ H ₅	Quant.
n-C ₃ H ₇	C ₆ H ₅	C ₆ H ₅	10d
n-C ₃ H ₇	C ₆ H ₅	C ₆ H ₅	393, 392
n-C ₃ H ₇	C ₆ H ₅	C ₆ H ₅	389
n-C ₃ H ₇	C ₆ H ₅	C ₆ H ₅	392
n-C ₃ H ₇	C ₆ H ₅	C ₆ H ₅	392
n-C ₃ H ₇	C ₆ H ₅	C ₆ H ₅	148
n-C ₃ H ₇	C ₆ H ₅	C ₆ H ₅	389
n-C ₃ H ₇	C ₆ H ₅	C ₆ H ₅	10d
n-C ₃ H ₇	C ₆ H ₅	C ₆ H ₅	393, 392
n-C ₃ H ₇	C ₆ H ₅	C ₆ H ₅	389
n-C ₃ H ₇	C ₆ H ₅	C ₆ H ₅	392
n-C ₃ H ₇	C ₆ H ₅	C ₆ H ₅	392
n-C ₃ H ₇	C ₆ H ₅	C ₆ H ₅	148

Note: References 177-180 are on pp. 136-142.

* Only the *syn* isomer of methyl glyoxalate 2,4-dimethylphenylhydrazone gave a formazan. The *anti* isomer reacted with the elimination of nitrogen.

† The phenylsulfonyl group was replaced by a phenyl group in the coupling reaction.

TABLE IX

COUPLING OF DIAZONIUM SALTS WITH HYDRAZONES

A. Simple Hydrazones

R	R'	RCH=NNHR' + R''N ₂ X →	$\begin{array}{c} \text{RC=NNHR}' \\ \\ \text{N=NR}'' \end{array}$	R''	Yield, %	References
H	Cholyl (C ₂₁ H ₃₉ O ₅)				—	387
O ₂ N	C ₆ H ₅			C ₆ H ₅	—	322
CH ₃	C ₆ H ₅			C ₆ H ₅	88	139, 144, 388
CH ₃	C ₆ H ₅			<i>o</i> -O ₂ NC ₆ H ₄	—	144
CH ₃	C ₆ H ₅			<i>m</i> -O ₂ NC ₆ H ₄	—	144
CH ₃	C ₆ H ₅			<i>p</i> -O ₂ NC ₆ H ₄	Quant.	139, 144
CH ₃	C ₆ H ₅			<i>p</i> -HO ₃ SC ₆ H ₄	Quant.	389
CH ₃	C ₆ H ₅			<i>p</i> -(C ₆ H ₅ CH=CH)C ₆ H ₄	68	389 <i>a</i>
CH ₃	C ₆ H ₅			<i>p</i> -(C ₆ H ₅ C(CN)=CH)C ₆ H ₄	—	389 <i>b</i>
CH ₃	C ₆ H ₅			<i>p</i> -(<i>p</i> -O ₂ NC ₆ H ₄ CH=CH)C ₆ H ₄	16	389 <i>a</i>
CH ₃	C ₆ H ₅			<i>p</i> -(<i>p</i> -CH ₃ CONHC ₆ H ₄ CH=CH)C ₆ H ₄	12	389 <i>a</i>
CH ₃	C ₆ H ₅			<i>p</i> -(C ₆ H ₅ N=N)C ₆ H ₄	28	389 <i>c</i>
CH ₃	<i>o</i> -O ₂ NC ₆ H ₄			<i>o</i> -O ₂ NC ₆ H ₄	Small	144
CH ₃	<i>p</i> -O ₂ NC ₆ H ₄			C ₆ H ₅	—	144
CH ₃	<i>p</i> -O ₂ NC ₆ H ₄			<i>o</i> -O ₂ NC ₆ H ₄	—	144
CH ₃	<i>p</i> -O ₂ NC ₆ H ₄			<i>m</i> -O ₂ NC ₆ H ₄	—	144
CH ₃	<i>p</i> -O ₂ NC ₆ H ₄			<i>p</i> -O ₂ NC ₆ H ₄	—	144
CH ₃	<i>p</i> -O ₂ NC ₆ H ₄			2,4-(O ₂ N) ₂ C ₆ H ₃	48	129, 144
CH ₃	2,4-(O ₂ N) ₂ C ₆ H ₃			C ₆ H ₅	—	390
CH ₃	2,4-(O ₂ N) ₂ C ₆ H ₃			<i>o</i> -O ₂ NC ₆ H ₄	—	391
CH ₃	2,4-(O ₂ N) ₂ C ₆ H ₃			<i>m</i> -O ₂ NC ₆ H ₄	—	390
CH ₃					—	390

C_6H_5	$p \text{ CH}_3\text{CONH}(\text{CH}_2)_{12}\text{N}(\text{COCH}_3)_2C_6H_5$	—	395a
C_6H_5	$p\text{-}[(C_6H_5)_2N(\text{CH}_2)_2O_2C]C_6H_5$	64	395a
C_6H_5	$p\text{-}\{(C_6H_5)_2N(\text{CH}_2)_2CH(\text{CH}_3)\text{NH}O_2S\}C_6H_5$	47	395a
C_6H_5	$p \text{ (C}_6\text{H}_5\text{CH=CH)C}_6\text{H}_5$	74	389a
C_6H_5	$p\text{-}(p \text{ HOC}_6\text{H}_4\text{CH=CH)C}_6\text{H}_5$	32	389a
C_6H_5	$p\text{-}(p\text{-BrC}_6\text{H}_4\text{CH=CH)C}_6\text{H}_5$	33	389a
C_6H_5	$p\text{-}(p\text{-O}_2\text{NC}_6\text{H}_4\text{CH=CH)C}_6\text{H}_5$	33	389a
C_6H_5	$p\text{-}(p\text{-CH}_3\text{CONHC}_6\text{H}_4\text{CH=CH)C}_6\text{H}_5$	14	389a
C_6H_5	$p\text{-}(C_6H_5N=N)C_6H_5$	50	389c
C_6H_5	$p\text{-}(p\text{-CH}_3C_6H_4N=N)C_6H_5$	53	389c
C_6H_5	$p\text{-}(p\text{-ClC}_6H_4N=N)C_6H_5$	12	389c
C_6H_5	$p\text{-}(p\text{-HOC}_6H_4N=N)C_6H_5$	28	389c
C_6H_5	$p\text{-}(p\text{-O}_2\text{NC}_6H_4N=N)C_6H_5$	57	389c
C_6H_5	$p\text{-}[p\text{-}(CH_3)_2\text{NC}_6H_4N=N]C_6H_5$	23	389c
C_6H_5	$p\text{-}(p \text{ CH}_3\text{CONHC}_6H_4N=N)C_6H_5$	35	389c
C_6H_5	$p\text{-}(2\text{-Cl-4-HOC}_6H_4N=N)C_6H_5$	27	389c
C_6H_5	$p \text{ (3-Cl-4-HOC}_6H_4N=N)C_6H_5$	8	389c
C_6H_5	2,5 $(\text{CH}_3)_2\text{-4-(C}_6\text{H}_5\text{N=N)C}_6\text{H}_5$	50	389c
C_6H_5	$\alpha \text{ C}_{10}\text{H}_7$	80	150, 147, 149, 390
C_6H_5	$\beta \text{-C}_{10}\text{H}_7$	47	150, 149, 390
C_6H_5	4-($C_6H_5N=N$) 1- $C_{10}H_8$	9	389c
C_6H_5	3-Pyridyl	53	395a
C_6H_5	6-Quinolyl	—	398a
C_6H_5	7-Quinolyl	—	398a
C_6H_5	6 Ethoxy-2 quinolyl	—	398a
C_6H_5	6 Methoxy 8-quinolyl	20	395a
C_6H_5	2 Quinolylmethyl	—	398a
C_6H_5	2 Thiazolyl	—	398a
C_6H_5	5-Methyl-2 thiazolyl	68	398b

Note: References 177-480 are on pp. 130-142

TABLE IX—Continued
A. Simple Hydrazones—Continued

R	R'	R''	Yield, %	References
$n\text{-C}_{11}\text{H}_{23}$	C_6H_5	$p\text{-BrC}_6\text{H}_4$	82	148
$n\text{-C}_{11}\text{H}_{23}$	C_6H_5	$p\text{-O}_2\text{NC}_6\text{H}_4$	83	148
$n\text{-C}_{11}\text{H}_{23}$	C_6H_5	$p\text{-HO}_2\text{SC}_6\text{H}_4$	Quant.	389
$n\text{-C}_{11}\text{H}_{23}$	C_6H_5	$\alpha\text{-C}_{10}\text{H}_7$	67	148
$n\text{-C}_{11}\text{H}_{23}$	$p\text{-BrC}_6\text{H}_4$	C_6H_5	63	148
$n\text{-C}_{11}\text{H}_{23}$	$p\text{-O}_2\text{NC}_6\text{H}_4$	C_6H_5	60	148
C_6H_5	C_6H_5	C_6H_5	50	394, 18, 19, 19a, 19b, 70 395
C_6H_5	C_6H_5	$p\text{-CH}_3\text{C}_6\text{H}_4$	—	19
C_6H_5	C_6H_5	$p\text{-i-C}_3\text{H}_7\text{C}_6\text{H}_4$	—	395a
C_6H_5	C_6H_5	$p\text{-n-C}_{12}\text{H}_{25}\text{C}_6\text{H}_4$	83	395a
C_6H_5	C_6H_5	$p\text{-ClC}_6\text{H}_4$	60	395a, 393
C_6H_5	C_6H_5	$p\text{-BrC}_6\text{H}_4$	50	18, 140
C_6H_5	C_6H_5	$p\text{-IC}_6\text{H}_4$	45–60	396
C_6H_5	C_6H_5	$o\text{-HOC}_6\text{H}_4$	80	303
C_6H_5	C_6H_5	$o\text{-O}_2\text{NC}_6\text{H}_4$	58	19b
C_6H_5	C_6H_5	$p\text{-O}_2\text{NC}_6\text{H}_4$	92	395a, 18
C_6H_5	C_6H_5	$p\text{-CH}_3\text{CONHC}_6\text{H}_4$	55	397
C_6H_5	C_6H_5	$o\text{-HO}_2\text{CC}_6\text{H}_4$	75	303
C_6H_5	C_6H_5	$p\text{-HO}_2\text{SC}_6\text{H}_4$	—	147
C_6H_5	C_6H_5	$p\text{-C}_6\text{H}_5\text{C}_6\text{H}_4$	44	395a, 398
C_6H_5	C_6H_5	$4\text{-CH}_3\text{CONH-2-ClC}_6\text{H}_3$	76	395a
C_6H_5	C_6H_5	$4\text{-CH}_3\text{CONH-3-ClC}_6\text{H}_3$	44	395a
C_6H_5	C_6H_5	$4\text{-CH}_3\text{CONH-2-O}_2\text{NC}_6\text{H}_3$	57	395a
C_6H_5	C_6H_5	$4\text{-CH}_3\text{CONH-2-CH}_3\text{CO}_2\text{C}_6\text{H}_3$	39	395a
C_6H_5	C_6H_5	$p\text{-n-C}_{12}\text{H}_{25}\text{CONHC}_6\text{H}_4$	—	395a

C_6H_5	$p-O_2NC_6H_4$	$\beta-C_{10}H_7$	390
C_6H_5	$p-O_2NC_6H_4$	$p-(p-C_6H_4OC_6H_4)_2C_6H_4$	398c
C_6H_5	$p-O_2NC_6H_4$	$3-CH_3O-4-(m-CH_3OC_6H_4)_2C_6H_4$	398c
C_6H_5	$p-O_2NC_6H_4$	$3-CH_3O-4-[3,4-(CH_3O)_2C_6H_3]C_6H_4$	398c
C_6H_5	$p-O_2NC_6H_4$	$2,5-(CH_3O)_2-4-(p-O_2NC_6H_4N=N)C_6H_4$	398c
C_6H_5	$o-HO_2CC_6H_4$	$o-HO_2CC_6H_4$	303
C_6H_5	$m-HO_2CC_6H_4$	C_6H_5	141
C_6H_5	$m-HO_2CC_6H_4$	$o-ClC_6H_4$	141
C_6H_5	$m-HO_2CC_6H_4$	$m-O_2NC_6H_4$	141
C_6H_5	$m-HO_2CC_6H_4$	$o-HO_2CC_6H_4$	141
C_6H_5	$m-HO_2CC_6H_4$	$m-HO_2CC_6H_4$	141
C_6H_5	$m-HO_2CC_6H_4$	$p-HO_2CC_6H_4$	141
C_6H_5	$p-HO_2CC_6H_4$	$p-(C_6H_4N=N)C_6H_4$	389c
C_6H_5	$p-CH_3CONHC_6H_4$	$p-(C_6H_4N=N)C_6H_4$	389c
C_6H_5	$p-HO_2SC_6H_4$	C_6H_5	147
C_6H_5	$(C_6H_4)_2NCO$	C_6H_5	19b
C_6H_5	$\alpha-C_{10}H_7$	C_6H_5	398d
C_6H_5	$\alpha-C_{10}H_7$	$p-CH_3C_6H_4$	147, 149, 390
C_6H_5	$\alpha-C_{10}H_7$	$p-O_2NC_6H_4$	390
C_6H_5	$\beta-C_{10}H_7$	C_6H_5	390
C_6H_5	$(\beta-C_{10}H_7)_2NCO$	C_6H_5	150, 149
C_6H_5	$p-C_6H_4(C_6H_4)NCO$	C_6H_5	398d
C_6H_5	$p-C_6H_4C_6H_4$	C_6H_5	398d
C_6H_5	Cholyl ($C_{27}H_{49}O_6$)	$p-C_6H_4C_6H_4$	398
C_6H_5	$p-(C_6H_4N=N)C_6H_4$	$p-(C_6H_4CH=CH)C_6H_4$	387
C_6H_5	2-Pyridyl	$p-ClC_6H_4$	389a
C_6H_5	2-Quinolyl	C_6H_5	398a
			19d

Note: References 177-480 are on pp 135-142.

‡ These products are probably 4-arylaazonaphthylhydrazones rather than formazans. See ref. 160.
 § A 35% yield of the 1-phenylaro-2 naphthylhydrazone of benzaldehyde was obtained also.

TABLE IX—Continued
A. Simple Hydrazones—Continued

R	R'	R''	Yield, %	References
C ₆ H ₅	C ₆ H ₅	4-Methyl-2-thiazolyl	1-3	398b
C ₆ H ₅	C ₆ H ₅	4,5-Dimethyl-2-thiazolyl	69	398b
C ₆ H ₅	C ₆ H ₅	2,5-Dimethyl-4-(2-thiazolylazo)phenyl	25	389c
C ₆ H ₅	C ₆ H ₅	p-(6-Methyl-2-benzothiazolyl)phenyl	—	398a
C ₆ H ₅	o-CH ₃ C ₆ H ₄	C ₆ H ₅	85	19b
C ₆ H ₅	o-CH ₃ C ₆ H ₄	p-O ₂ NC ₆ H ₄	37	19b
C ₆ H ₅	p-CH ₃ C ₆ H ₄	C ₆ H ₅	—	19
C ₆ H ₅	p-CH ₃ C ₆ H ₄	p-CH ₃ C ₆ H ₄	—	19
C ₆ H ₅	p-CH ₃ C ₆ H ₄	α-C ₁₀ H ₇	—	390
C ₆ H ₅	p-CH ₃ C ₆ H ₄	β-C ₁₀ H ₇	—	390
C ₆ H ₅	o-CH ₃ OC ₆ H ₄	o-CH ₃ OC ₆ H ₄	—	290a
C ₆ H ₅	p-CH ₃ OC ₆ H ₄	p-CH ₃ OC ₆ H ₄	60	290a
C ₆ H ₅	o-C ₃ H ₅ OC ₆ H ₄	C ₆ H ₅	91	19b
C ₆ H ₅	o-C ₃ H ₅ OC ₆ H ₄	p-O ₂ NC ₆ H ₄	51	19b
C ₆ H ₅	p-C ₃ H ₅ OC ₆ H ₄	C ₆ H ₅	74	19b
C ₆ H ₅	o-ClC ₆ H ₄	C ₆ H ₅	26	19b
C ₆ H ₅	p-ClC ₆ H ₄	C ₆ H ₅	55	19b
C ₆ H ₅	p-ClC ₆ H ₄	p-ClC ₆ H ₄	50	19b
C ₆ H ₅	p-ClC ₆ H ₄	p-(C ₆ H ₅ N=N)C ₆ H ₄	18	19b
C ₆ H ₅	p-BrC ₆ H ₄	C ₆ H ₅	50	18, 149
C ₆ H ₅	p-IC ₆ H ₄	p-IC ₆ H ₄	42-51	396
C ₆ H ₅	o-C ₂ NC ₆ H ₄	C ₆ H ₅	10	19b
C ₆ H ₅	p-O ₂ NC ₆ H ₄	C ₆ H ₅	46	19b
C ₆ H ₅	p-O ₂ NC ₆ H ₄	p-IC ₆ H ₄	30-58	396
C ₆ H ₅	p-O ₂ NC ₆ H ₄	p-O ₂ NC ₆ H ₄	8	323b
C ₆ H ₅	p-O ₂ NC ₆ H ₄	p-O ₂ NC ₆ H ₄	22	398c
C ₆ H ₅	p-O ₂ NC ₆ H ₄	α-C ₁₀ H ₇	41	150, 390

$p\text{-NCC}_6\text{H}_4$	C_6H_5	C_6H_5	65	395a
$p\text{-NCC}_6\text{H}_4$	C_6H_5	$p\text{-NCC}_6\text{H}_4$	80	395a
$o\text{-O}_2\text{NC}_6\text{H}_4$	2-Pyridyl	$p\text{-ClC}_6\text{H}_4$	—	398a
$o\text{-O}_2\text{NC}_6\text{H}_4$	2-Quinolyl	$p\text{-ClC}_6\text{H}_4$	—	398a
$p\text{-O}_2\text{NC}_6\text{H}_4$	C_6H_5	C_6H_5	40	10b, 395a
$p\text{-O}_2\text{NC}_6\text{H}_4$	$p\text{-CH}_3\text{OC}_6\text{H}_4$	$p\text{-CH}_3\text{OC}_6\text{H}_4$	51	323b
$p\text{-O}_2\text{NC}_6\text{H}_4$	$p\text{-O}_2\text{NC}_6\text{H}_4$	$p\text{-C}_6\text{H}_5\text{C}_6\text{H}_4$	49	398c
$p\text{-O}_2\text{NC}_6\text{H}_4$	$p\text{-O}_2\text{NC}_6\text{H}_4$	$3\text{-CH}_3\text{O}-4\text{-(}m\text{-CH}_3\text{OC}_6\text{H}_4\text{)}\text{C}_6\text{H}_4$	23	398c
$p\text{-O}_2\text{NC}_6\text{H}_4$	$\text{H}_2\text{N(HN=)C}$	C_6H_5	—	402
$p\text{-HO}_2\text{CC}_6\text{H}_4$	$p\text{-(C}_6\text{H}_5\text{N=N)C}_6\text{H}_4$	$p\text{-(C}_6\text{H}_5\text{CH=CH)C}_6\text{H}_4$	53	389a
$p\text{CH}_3\text{CO}_2\text{C}_6\text{H}_4$	$p\text{-(C}_6\text{H}_5\text{N=N)C}_6\text{H}_4$	$p\text{-(C}_6\text{H}_5\text{CH=CH)C}_6\text{H}_4$	40	389a
$p\text{-CH}_3\text{CONHC}_6\text{H}_4$	C_6H_5	C_6H_5	53	395a
$p\text{CH}_3\text{CONHC}_6\text{H}_4$	C_6H_5	$p\text{-CH}_3\text{CONHC}_6\text{H}_4$	17	395a
$p\text{-CH}_3\text{CONHC}_6\text{H}_4$	$p\text{-CH}_3\text{CONHC}_6\text{H}_4$	$p\text{-(}p\text{-HOC}_6\text{H}_4\text{N=N)C}_6\text{H}_4$	—	389c
$m\text{-HO}_2\text{SC}_6\text{H}_4$	C_6H_5	C_6H_5	—	147
$3,4\text{-(CH}_3\text{O)}_2\text{C}_6\text{H}_3$	C_6H_5	$p\text{-CH}_3\text{OC}_6\text{H}_4$	25	395a
$\text{C}_6\text{H}_4\text{CH}_3$	Cholyl ($\text{C}_{11}\text{H}_{19}\text{O}_4$)	C_6H_5	—	387
$\text{C}_6\text{H}_4\text{CO}$	C_6H_5	C_6H_5	—	70, 204
$p\text{-C}_6\text{H}_5\text{C}_6\text{H}_4$	C_6H_5	C_6H_5	43	398
$p\text{-C}_6\text{H}_5\text{C}_6\text{H}_4$	$p\text{-C}_6\text{H}_5\text{C}_6\text{H}_4$	$p\text{-C}_6\text{H}_5\text{C}_6\text{H}_4$	23	398
2-Furyl	C_6H_5	C_6H_5	14	402a
2-Furyl	$(\text{C}_6\text{H}_5)_2\text{NCO}$	C_6H_5	—	398d
2-Furyl	2-Pyridyl	$p\text{-ClC}_6\text{H}_4$	—	398a
2-Furyl	2-Quinolyl	$p\text{-ClC}_6\text{H}_4$	—	398a
2-Furyl	Cholyl ($\text{C}_{11}\text{H}_{19}\text{O}_4$)	C_6H_5	—	387
2-Thienyl	C_6H_5	$m\text{-F}_2\text{OC}_6\text{H}_4$	—	398a
2-Pyridyl	C_6H_5	C_6H_5	—	398a
2-Pyridyl	C_6H_5	$p\text{-CH}_3\text{OC}_6\text{H}_4$	46	402a
2-Pyridyl	C_6H_5	$p\text{-ClC}_6\text{H}_4$	95	402a
2-Pyridyl	C_6H_5	$o\text{-H}_1\text{NC}_6\text{H}_4$	40	402a
2-Pyridyl	C_6H_5		35	402b

Note: References 177-480 are on pp. 136-142.

TABLE IX—Continued
A. Simple Hydrazones—Continued

R	R'	R''	Yield, %	References
C_6H_5	2-Quinolyl	$p-ClC_6H_5$	—	398a
C_6H_5	2-Thiazolyl	C_6H_5	66	398b
C_6H_5	4-Methyl-2-thiazolyl	C_6H_5	50	398b
C_6H_5	4-Phenyl-2-thiazolyl	C_6H_5	38	398b
C_6H_5	4,5-Diphenyl-2-thiazolyl	C_6H_5	22	398b
C_6H_5	$H_2N(NH=)C$	C_6H_5	61	402
C_6H_5	$H_2N(HN=)C$	$m-O_2NC_6H_4$	—	402
$p-(CH_3)_2CHC_6H_4$	$H_2N(HN=)C$	5-Tetrazolyl	—	19d
$p-CH_3OC_6H_4$	C_6H_5	C_6H_5	—	15
$p-CH_3OC_6H_4$	C_6H_5	$p-(C_6H_5CH=CH)C_6H_4$	83	389a
$p-CH_3OC_6H_4$	$p-ClC_6H_4$	$p-ClC_6H_4$	43	323b
$p-CH_3OC_6H_4$	$p-O_2NC_6H_4$	$p-O_2NC_6H_4$	15	323b
$p-CH_3OC_6H_4$	2-Pyridyl	$p-ClC_6H_4$	—	398a
$p-CH_3OC_6H_4$	2-Quinolyl	$p-ClC_6H_4$	—	398a
$p-CH_3OC_6H_4$	$H_2N(NH=)C$	5-Tetrazolyl	—	19d
$o-ClC_6H_4$	2-Pyridyl	5-Tetrazolyl	—	398a
$o-ClC_6H_4$	2-Quinolyl	5-Tetrazolyl	—	398a
$p-ClC_6H_4$	$o-CH_3OC_6H_4$	$o-CH_3OC_6H_4$	44	323b
$p-ClC_6H_4$	$H_2N(NH=)C$	5-Tetrazolyl	—	19d
$p-BrC_6H_4$	C_6H_5	$p-BrC_6H_4$	80	395a
$p-BrC_6H_4$	C_6H_5	2,4,6- $Br_3C_6H_3$	10	395a
$p-BrC_6H_4$	$(C_6H_5)_2NCO$	$p-(C_6H_5CH=CH)C_6H_4$	47	389a
$o-HOC_6H_4$	2-Pyridyl	C_6H_5	—	398d
$o-HOC_6H_4$	2-Quinolyl	$p-ClC_6H_4$	—	398a
$p-HOC_6H_4$	C_6H_5	$p-ClC_6H_4$	—	398a
		$p-(C_6H_5N=N)C_6H_4$	50	389a

B. Hydrazones of Sugars

Hydrazone	Substituent in Aniline	Product (Yield, %)	References
D-Glucose phenylhydrazone	—	D-Glucose diphenylformazan (64)	139b, 139c
D-Glucose phenylosazone	—	D Glucose phenylosazone (20)	139d
Anhydro D glucose phenylosazone	—	Anhydro-D-glucose phenylosazone formazan (27)	139d
D-Galactose phenylhydrazone	—	D Galactose diphenylformazan (73)	139b, 139c, 139e
D-Galactose p bromophenylhydrazone	4-Bromo	D-Galactose phenyl (p-bromophenyl)formazan	139f
D-Galactose phenylhydrazone	—	D Galactose phenyl-(p bromophenyl)formazan	139f
D-Mannose phenylhydrazone	—	D-Mannose diphenylformazan (68)	139b, 139c
L-Arabinose phenylhydrazone	—	L-Arabinose diphenylformazan (51)	139b
L-Rhamnose phenylhydrazone	—	L-Rhamnose diphenylformazan (45)	139b, 139e
D-Xylose phenylhydrazone	—	D-Xylose diphenylformazan (55)	139b
D-Mannose pentaacetate phenylhydrazone	—	D-Mannose diphenylformazan pentaacetate (57)	139e

Note: References 177-480 are on pp. 136-142.

TABLE IX—Continued
A. Simple Hydrazones—Continued

R	R'	R''	Yield, %	References
2-Pyridyl	C ₆ H ₅	<i>p</i> -(C ₆ H ₅ CH=CH)C ₆ H ₄	40	402a
2-Pyridyl	C ₆ H ₅	<i>p</i> -(C ₆ H ₅ N=N)C ₆ H ₄	39	402a
2-Pyridyl	2-Pyridyl	<i>p</i> -ClC ₆ H ₄	—	398a
2-Pyridyl	2-Quinolyl	<i>p</i> -ClC ₆ H ₄	—	398a
2-Pyridyl	2-Quinolyl	6-Quinolyl	—	398a
4-Pyridyl	2-Quinolyl	<i>p</i> -ClC ₆ H ₄	—	398a
4-Pyridyl	2-Quinolyl	6-Quinolyl	—	398a
2-Phenyl-1,2,3,4-tiazol-4-yl	C ₆ H ₅	C ₆ H ₅	—	398a
2,6-Dioxo-4-pyrimidyl	C ₆ H ₅	C ₆ H ₅	50	402a
2-Quinolyl	C ₆ H ₅	C ₆ H ₅	76	399
2-Quinolyl	C ₆ H ₅	C ₆ H ₅	50	402d, 139a
2-Benzothiazolyl	C ₆ H ₅	<i>o</i> -HO ₂ CC ₆ H ₄	65	400, 402e
2-Benzothiazolyl	C ₆ H ₅	C ₆ H ₅	47	402d, 402f,
				402g
2-Benzothiazolyl	C ₆ H ₅	<i>p</i> -ClC ₆ H ₄	—	132b, 402f
		<i>p</i> -O ₂ NC ₆ H ₄	—	132b, 402f,
				402h
2-Benzothiazolyl	C ₆ H ₅	<i>o</i> -HO ₂ CC ₆ H ₄	50	402d
2-Benzothiazolyl	<i>p</i> -ClC ₆ H ₄	C ₆ H ₅	—	132b, 402f
2-Benzothiazolyl	<i>p</i> -ClC ₆ H ₄	<i>p</i> -ClC ₆ H ₄	—	132b, 402f
2-Benzothiazolyl	<i>p</i> -O ₂ NC ₆ H ₄	C ₆ H ₅	—	132b, 402f,
				402h
2-Benzothiazolyl	<i>p</i> -O ₂ NC ₆ H ₄	<i>p</i> -O ₂ NC ₆ H ₄	—	132b, 402f,
				402i
2-Benzofurquinolyl	C ₆ H ₅	C ₆ H ₅	48	402i
2-Benzofurquinolyl	C ₆ H ₅	<i>o</i> -HO ₂ CC ₆ H ₄	65	402i

TABLE IX—Continued
C. Diformazans from Hydrazones and Diamines

$\text{RCH=NNHR}' + \text{XN}_2\text{C}_6\text{H}_3\text{Y} \rightarrow \left[\text{RC=NNHR}' \right]_2$			
R	R'	Y	Yield, %
CH ₃	C ₆ H ₅	H	—
C ₆ H ₅	C ₆ H ₅	H	90
C ₆ H ₅	C ₆ H ₅	CH ₃	39
C ₆ H ₅	C ₆ H ₅	CH ₃ O	72¶
C ₆ H ₅	C ₆ H ₅	H	11
C ₆ H ₅	<i>p</i> -O ₂ NC ₆ H ₄	CH ₃ O	18
C ₆ H ₅	<i>p</i> -O ₂ NC ₆ H ₄	CH ₃ O	—
C ₆ H ₅	2-Pyridyl	CH ₃ O	—
C ₆ H ₅	2-Quinolyl	CH ₃ O	—
<i>p</i> -CH ₃ OC ₆ H ₄	C ₆ H ₅	CH ₃ O	—
<i>o</i> -ClC ₆ H ₄	2-Pyridyl	CH ₃ O	—
<i>o</i> -ClC ₆ H ₄	2-Quinolyl	CH ₃ O	—
<i>o</i> -HOC ₆ H ₄	C ₆ H ₅	CH ₃ O	—
<i>o</i> -O ₂ NC ₆ H ₄	2-Pyridyl	CH ₃ O	—
<i>o</i> -O ₂ NC ₆ H ₄	2-Quinolyl	CH ₃ O	—
<i>p</i> -O ₂ NC ₆ H ₄	<i>p</i> -O ₂ NC ₆ H ₄	CH ₃ O	—
<i>p</i> -O ₂ NC ₆ H ₄	<i>p</i> -O ₂ NC ₆ H ₄	H	49
3,4-(CH ₃ O) ₂ C ₆ H ₃	C ₆ H ₅	CH ₃ O	12
2-Furyl	C ₆ H ₅	CH ₃ O	79
2-Furyl	2-Pyridyl	CH ₃ O	70
2-Furyl	2-Quinolyl	CH ₃ O	—

References
 179
 402j
 402j
 402k, 402j
 398c
 398c
 398a
 398a
 402k
 398a
 398a
 402k
 398a
 398c
 398c
 402k
 402k, 398a
 398a
 398a

Cl	HO ₂ C	<i>o</i> -CH ₃ O ₂ CC ₆ H ₄	<i>p</i> -O ₂ NC ₆ H ₄	—	145
Cl	HO ₂ C	2,4-(CH ₃) ₂ C ₆ H ₃	<i>p</i> -O ₂ NC ₆ H ₄	—	145
CH ₃	HO ₂ C	C ₆ H ₅	C ₆ H ₅	87-89	27, 153, 95a
CH ₃	HO ₂ C	C ₆ H ₅	<i>o</i> -O ₂ NC ₆ H ₄	—	144
CH ₃	HO ₂ C	<i>o</i> -CH ₃ OC ₆ H ₄	<i>o</i> CH ₃ OC ₆ H ₄	70	290a
CH ₃	HO ₂ C	<i>p</i> CH ₃ OC ₆ H ₄	<i>p</i> -CH ₃ OC ₆ H ₄	—	290a
CH ₃ O ₂ C	HO ₂ C	C ₆ H ₅	C ₆ H ₅	—	70
C ₂ H ₅ O ₂ C	HO ₂ C	C ₆ H ₅	C ₆ H ₅	Quant.	70
C ₂ H ₅ O ₂ C	HO ₂ C	C ₆ H ₅	<i>p</i> -CH ₃ C ₆ H ₄	—	19
CH ₃ CO	HO ₂ C	C ₆ H ₅	C ₆ H ₅	75	52, 142
C ₆ H ₅	HO ₂ C	C ₆ H ₅	C ₆ H ₅	—	19
C ₆ H ₅	HO ₂ C	C ₆ H ₅	<i>o</i> -CH ₃ C ₆ H ₄	—	141
C ₆ H ₅	HO ₂ C	C ₆ H ₅	<i>o</i> -O ₂ NC ₆ H ₄	—	141
C ₆ H ₅	HO ₂ C	C ₆ H ₅	<i>m</i> O ₂ NC ₆ H ₄	—	141
C ₆ H ₅	HO ₂ C	C ₆ H ₅	<i>p</i> -O ₂ NC ₆ H ₄	—	141
C ₆ H ₅	HO ₂ C	C ₆ H ₅	2,4-(CH ₃) ₂ C ₆ H ₃	—	141
C ₆ H ₅	HO ₂ C	C ₆ H ₅	C ₆ H ₅	—	120
C ₆ H ₅	HO ₂ C	C ₆ H ₅	C ₆ H ₅	56	60, 70, 140, 151
C ₆ H ₅	HO ₂ C	C ₆ H ₅	<i>p</i> -CH ₃ C ₆ H ₄	—	19
<i>p</i> -CH ₃ C ₆ H ₄	HO ₂ C	<i>p</i> -CH ₃ C ₆ H ₄	C ₆ H ₅	—	19
<i>o</i> -CH ₃ C ₆ H ₄	HO ₂ C	<i>o</i> -CH ₃ C ₆ H ₄	<i>o</i> -ClC ₆ H ₄	23	403a
<i>o</i> -ClC ₆ H ₄	HO ₂ C	<i>o</i> -ClC ₆ H ₄	<i>o</i> -CH ₃ C ₆ H ₄	7	403a
<i>o</i> -ClC ₆ H ₄	HO ₂ C	<i>o</i> -ClC ₆ H ₄	<i>o</i> -ClC ₆ H ₄	38	403a
<i>o</i> -O ₂ NC ₆ H ₄	HO ₂ C	<i>o</i> -O ₂ NC ₆ H ₄	<i>o</i> -O ₂ NC ₆ H ₄	4	403a

Note: References 177-180 are on pp. 138-142.

.. The starting material was the hydrazone of α -oxo- γ -butyrolactone.

TABLE IX—Continued

E. Diformazans from Dibenzalaminoguanidines

$\text{RCH=NNHC(=NH)NHN=CHR} + 2\text{R}'\text{N}_2\text{X} \rightarrow \text{RC=NNHC(=NH)NHN=CR}$ $\begin{array}{c} \text{N=NR}' \\ \text{R}'\text{N=N} \end{array}$			
R	R'	References	
C ₆ H ₅	C ₆ H ₅	403	
C ₆ H ₅	<i>o</i> -O ₂ NC ₆ H ₄	19 <i>d</i>	
C ₆ H ₅	<i>p</i> -O ₂ NC ₆ H ₄	19 <i>d</i>	
C ₆ H ₅	<i>p</i> -HO ₂ SC ₆ H ₄	403	
C ₆ H ₅	4-CH ₃ -2-(O ₂ N)C ₆ H ₃	19 <i>d</i>	
C ₆ H ₅	2-CH ₃ -6-(O ₂ N)C ₆ H ₃	19 <i>d</i>	
C ₆ H ₅	2-CH ₃ -4-ClC ₆ H ₃	19 <i>d</i>	
C ₆ H ₅	β-C ₁₀ H ₇	19 <i>d</i>	
C ₆ H ₅	4-Antipyril	19 <i>d</i>	
<i>m</i> -O ₂ NC ₆ H ₄	C ₆ H ₅	403	

F. Hydrazones Which Couple with Elimination of a Substituent

$\text{RC=NNHR}'' + \text{R}'''\text{N}_2\text{X} \xrightarrow{\text{OH}^-} \text{RC=NNHR}'' + \text{R}'\text{OH}$ $\begin{array}{c} \text{R}' \\ \text{R}' \end{array} \quad \begin{array}{c} \text{R}'' \\ \text{N=NR}'' \end{array}$			
R	R'	R''	References
H	HO ₂ C	C ₆ H ₅	143
H	HO ₂ C	2,4-Br ₂ C ₆ H ₃	170 <i>a</i>
Cl	HO ₂ C	<i>p</i> -O ₂ NC ₆ H ₄	145
		Yield, %	
		20	
		—	
		Quant.	

TABLE X

COUPLING OF DIAZONIUM SALTS WITH HETEROCYCLIC COMPOUNDS

1. *5-Pyrazolones*

Heterocyclic Compound,
Substituent(s) in



Substituent(s)
in Aniline*



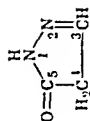
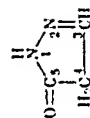
Product (Yield, %),
Substituent(s) in

—	—	4-Phenylazo (quant.)	References 405, 404
3-Methyl	4-Methyl	4-(<i>p</i> -Tolylazo) (quant.)	405, 404, 403, 407
—	—	3-Methyl-1-phenylazo	404, 407, 408
2-Aminoanthra- quinone	2-Aminoanthra- quinone	3-Methyl-4-(2-anthraquinonylazo) (quant.)	250
3 Carboxy	—	3-Carboxy-4-phenylazo	404
3 Carboxymethoxy	2-Carboxy	3-Carboxy-4-(<i>o</i> -carboxyphenylazo)	404
3 Carbethoxy	2-Carbethoxy	3-Carboxy-4-(<i>o</i> -carbethoxyphenylazo)	400
—	—	3-Carboethoxy-4-phenylazo	404
2-Carboxy	2-Carboxy	3-Carboethoxy-4-phenylazo	404
2 Carbethoxy	2 Carbethoxy	3-Carboethoxy-4-(<i>o</i> -carboxyphenylazo)	404
4-Methyl	4-Methyl	3-Carboethoxy-4-(<i>o</i> -carboethoxyphenylazo)	401
—	—	3-Phenyl-4-phenylazo	400
4-Methyl	4-Methyl	3-Phenyl-4-(<i>o</i> -tolylazo)	85
α-Naphthylamine	α-Naphthylamine	3-Phenyl-4-(<i>p</i> -tolylazo)	404, 407, 408, 400
β-Naphthylamine	β-Naphthylamine	3-Phenyl-4-(<i>β</i> -naphthylazo)	404, 400

Note. References 177-180 are on pp. 130-142.
* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

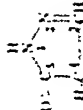

TABLE X—Continued
 4. 5-Pyrazolones—Continued

Heterocyclic Compound,
 Substituent(s) in



Substituent(s) in	Product (Yield, %), Substituent(s) in	References
Substituent(s) in Aniline*		
—	3-(2-Furyl)-4-phenylazo	410
4-Methoxy	1-Methyl-3-amino-4-(<i>p</i> -anisylazo) (41)	411
4-Methoxy	1-Methyl-3-carbethoxy-4-(<i>p</i> -anisylazo) (58)	411
—	1-Methyl-3-phenyl-4-phenylazo	412
—	1-Acetyl-3-phenyl-4-phenylazo	408
—	1-Phenyl-4-phenylazo	157
—	1-Phenyl-3-methyl-4-phenylazo	413, 414, 415
2-Methyl	1-Phenyl-3-methyl-4-(<i>o</i> -tolylazo)	415, 416, 417
3-Methyl	1-Phenyl-3-methyl-4-(<i>m</i> -tolylazo)	415, 417
4-Methyl	1-Phenyl-3-methyl-4-(<i>p</i> -tolylazo)	415, 417
2-Methoxy	1-Phenyl-3-methyl-4-(<i>o</i> -anisylazo)	415, 417
4-Methoxy	1-Phenyl-3-methyl-4-(<i>p</i> -anisylazo)	415, 417
2-Ethoxy	1-Phenyl-3-methyl-4-(<i>o</i> -ethoxyphenylazo)	415, 417
4-Ethoxy	1-Phenyl-3-methyl-4-(<i>p</i> -ethoxyphenylazo)	415, 417
2-Chloro	1-Phenyl-3-methyl-4-(<i>o</i> -chlorophenylazo)	68, 415
3-Chloro	1-Phenyl-3-methyl-4-(<i>m</i> -chlorophenylazo)	415
4-Chloro	1-Phenyl-3-methyl-4-(<i>p</i> -chlorophenylazo)	415, 417
4-Bromo	1-Phenyl-3-methyl-4-(<i>p</i> -bromophenylazo)	415, 417
4-Acetyl	1-Phenyl-3-methyl-4-(<i>p</i> -acetylphenylazo)	417
2-Nitro	1-Phenyl-3-methyl-4-(<i>o</i> -nitrophenylazo)	415, 417
3-Nitro	1-Phenyl-3-methyl-4-(<i>m</i> -nitrophenylazo)	415, 417

TABLE X—Continued
A. *5-Pyrazolones—Continued*

Heterocyclic Compound, Substituent(s) in	Product (Yield, %), Substituent(s) in	References
		
1-Phenyl-3-carbethoxymethyl	1-Phenyl-3-carbethoxymethyl-4-(<i>p</i> -tolylazo) (89)	65
1,3-Diphenyl	1-Phenyl-3-carbethoxymethyl-4-(<i>p</i> -nitrophenylazo) (85)	65
	1,3-Diphenyl-4-phenylazo	409, 415, 422
	1,3-Diphenyl-4-(<i>o</i> -tolylazo)	409, 415
3-Methyl	1,3-Diphenyl-4-(<i>m</i> -tolylazo)	415
4-Methyl	1,3-Diphenyl-4-(<i>p</i> -tolylazo)	409, 415
2-Methoxy	1,3-Diphenyl-4-(<i>o</i> -anisylazo)	415
4-Methoxy	1,3-Diphenyl-4-(<i>p</i> -anisylazo)	415
2-Ethoxy	1,3-Diphenyl-4-(<i>o</i> -ethoxyphenylazo)	415
4-Ethoxy	1,3-Diphenyl-4-(<i>p</i> -ethoxyphenylazo)	415
2-Chloro	1,3-Diphenyl-4-(<i>o</i> -chlorophenylazo)	415
3-Chloro	1,3-Diphenyl-4-(<i>m</i> -chlorophenylazo)	415
4-Chloro	1,3-Diphenyl-4-(<i>p</i> -chlorophenylazo)	415
4-Bromo	1,3-Diphenyl-4-(<i>p</i> -bromophenylazo)	415
2-Nitro	1,3-Diphenyl-4-(<i>o</i> -nitrophenylazo)	415
3-Nitro	1,3-Diphenyl-4-(<i>m</i> -nitrophenylazo)	415
4-Nitro	1,3-Diphenyl-4-(<i>p</i> -nitrophenylazo)	415
3-Sulfo	1,3-Diphenyl-4-(<i>m</i> -sulfophenylazo)	418
4-Sulfo	1,3-Diphenyl-4-(<i>p</i> -sulfophenylazo)	418
2,5-Dichloro	1,3-Diphenyl-4-(2,5-dichlorophenylazo)	415
4-Chloro-2-methyl	1,3-Diphenyl-4-(4-chloro-2-methylphenylazo)	415

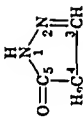
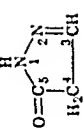
5-Chloro-2-methyl	1,2-Diphenyl-1-4-(5-chloro-2-methylphenylazo)	415
4-Chloro-2-nitro	1,2-Diphenyl-1-4-(4-chloro-2-nitrophenylazo)	415
3-Methyl-4-sulfo	1,2-Diphenyl-1-4-(3-methyl-4-sulphophenylazo)	418
4-Chloro-3-sulfo	1,2-Diphenyl-1-4-(4-chloro-3-sulphophenylazo)	418
α -Naphthylamine	1,2-Diphenyl-1-4-(α -naphthylazo)	409, 415
β -Naphthylamine	1,2-Diphenyl-1-4-(β -naphthylazo)	409, 415
1-sulfo-2-naphthylamine	1,2-Diphenyl-1-4-(1-sulfo-2-naphthylazo)	418
1-Phenyl-3-(2-furyl)	1-Phenyl-3-(2-furyl)-4-(phenylazo)	410, 415
2-Methyl	1-Phenyl-3-(2-furyl)-4-(methylazo)	410, 415
3-Methyl	1-Phenyl-3-(2-furyl)-4-(methylazo)	410, 415
4-Methyl	1-Phenyl-3-(2-furyl)-4-(methylazo)	410, 415
2-Methoxy	1-Phenyl-3-(2-furyl)-4-(methoxyazo)	410, 415
4-Methoxy	1-Phenyl-3-(2-furyl)-4-(methoxyazo)	410, 415
2-Ethoxy	1-Phenyl-3-(2-furyl)-4-(ethoxyazo)	410, 415
4-Ethoxy	1-Phenyl-3-(2-furyl)-4-(ethoxyazo)	410, 415
2-Chloro	1-Phenyl-3-(2-furyl)-4-(2-chlorophenylazo)	410, 415
3-Chloro	1-Phenyl-3-(2-furyl)-4-(3-chlorophenylazo)	410, 415
4-Chloro	1-Phenyl-3-(2-furyl)-4-(4-chlorophenylazo)	410, 415
4-Bromo	1-Phenyl-3-(2-furyl)-4-(4-bromophenylazo)	410, 415
2-Nitro	1-Phenyl-3-(2-furyl)-4-(2-nitrophenylazo)	410, 415
3-Nitro	1-Phenyl-3-(2-furyl)-4-(3-nitrophenylazo)	410, 415
4-Nitro	1-Phenyl-3-(2-furyl)-4-(4-nitrophenylazo)	410, 415
3-Sulfo	1-Phenyl-3-(2-furyl)-4-(3-sulphophenylazo)	410, 415
4-Sulfo	1-Phenyl-3-(2-furyl)-4-(4-sulphophenylazo)	418
2,5-Dichloro	1-Phenyl-3-(2-furyl)-4-(2,5-dichlorophenylazo)	418
4-Chloro-2-methyl	1-Phenyl-3-(2-furyl)-4-(4-chloro-2-methylphenylazo)	415
5-Chloro-2-methyl	1-Phenyl-3-(2-furyl)-4-(5-chloro-2-methylphenylazo)	415
4-Chloro-2-nitro	1-Phenyl-3-(2-furyl)-4-(4-chloro-2-nitrophenylazo)	415

Note: References 177-480 are on pp. 130-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

TABLE X—Continued

4. 5-Pyrazolones—Continued

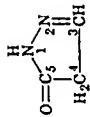
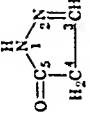
Heterocyclic Compound, Substituent(s) in	Product (Yield, %), Substituent(s) in	References
		
1-Phenyl-3-(2-furyl) (Cont.)	Substituent(s) in Aniline*	
	3-Methyl-4-sulfo	1-Phenyl-3-(2-furyl)-4-(3-methyl-4-sulphophenylazo) 418
	4-Chloro-3-sulfo	1-Phenyl-3-(2-furyl)-4-(4-chloro-3-sulphophenylazo) 418
	α -Naphthylamine	1-Phenyl-3-(2-furyl)-4-(α -naphthylazo) 415
	β -Naphthylamine	1-Phenyl-3-(2-furyl)-4-(β -naphthylazo) 410, 415
	1-Sulfo-2-naphthylamine	1-Phenyl-3-(2-furyl)-4-(1-sulfo-2-naphthylazo) 418
	4-Methoxy	1-Phenyl-3-(α -phenylbutyramido)-4-(<i>p</i> -anisylazo) (80) 423
	—	1- <i>p</i> -Tolyl-3-methyl-4-phenylazo 416
	4-Methyl	1- <i>p</i> -Tolyl-3-methyl-4-(<i>p</i> -tolylazo) 416
	2-Chloro	1-(<i>o</i> -Chlorophenyl)-3-methyl-4-(<i>o</i> -chlorophenylazo) 424
	2,4-Dichloro	1-(<i>m</i> -Chlorophenyl)-3-methyl-4-(2,4-dichlorophenylazo) 424
	4-Chloro	1-(<i>p</i> -Chlorophenyl)-3-methyl-4-(<i>p</i> -chlorophenylazo) 424
	—	1-(2,4-Dichlorophenyl)-3-methyl-4-phenylazo 424
	—	1-(<i>m</i> -Nitrophenyl)-3-phenyl-4-phenylazo 425
	4-Methoxy	1-(<i>p</i> -Nitrophenyl)-3-methyl-4-(<i>p</i> -anisylazo) (52) 423
	2-Chloro	1-(<i>p</i> -Nitrophenyl)-3-methyl-4-(<i>o</i> -chlorophenylazo) 68
	—	1-(<i>o</i> -Carboxyphenyl)-3-methyl-4-phenylazo 426
	—	1-(<i>o</i> -Carboxyphenyl)-3-phenyl-4-phenylazo 427
	4-Methyl	1-(<i>o</i> -Carboxyphenyl)-3-phenyl-4-(<i>p</i> -tolylazo) 427

1-(<i>m</i> -Carboxyphenyl)-3-methyl	1-(<i>m</i> -Carboxyphenyl)-3-methyl-4-phenylazo	428
1-(<i>p</i> -Carboxyphenyl)-3-methyl	1-(<i>p</i> -Carboxyphenyl)-3-methyl-4-phenylazo	428
1-(<i>o</i> -Sulfophenyl)-3-methyl	1-(<i>o</i> -Sulfophenyl)-3-methyl-4-phenylazo	429
1-(<i>p</i> -Sulfophenyl)-3-methyl	1-(<i>p</i> -Sulfophenyl)-3-methyl-4-phenylazo	430, 431
4-Nitro	1-(<i>p</i> -Sulfophenyl)-3-methyl-4-(<i>p</i> -nitrophenylazo)	430, 432
2,5-Dichloro	1-(<i>p</i> -Sulfophenyl)-3-methyl-4-(2,5-dichlorophenylazo)	430
4-Chloro-2-methyl	1-(<i>p</i> -Sulfophenyl)-3-methyl-4-(4-chloro-2-methylphenylazo)	430
5-Chloro-2-methyl	1-(<i>p</i> -Sulfophenyl)-3-methyl-4-(5-chloro-2-methylphenylazo)	430
1-(<i>p</i> -Sulfophenyl)-3-phenyl	1-(<i>p</i> -Sulfophenyl)-3-phenyl-4-phenylazo	430
2-Nitro	1-(<i>p</i> -Sulfophenyl)-3-phenyl-4-(<i>o</i> -nitrophenylazo)	430
4-Nitro	1-(<i>p</i> -Sulfophenyl)-3-phenyl-4-(<i>p</i> -nitrophenylazo)	430
2,5-Dichloro	1-(<i>p</i> -Sulfophenyl)-3-phenyl-4-(2,5-dichlorophenylazo)	430
4-Chloro-2-methyl	1-(<i>p</i> -Sulfophenyl)-3-phenyl-4-(4-chloro-2-methylphenylazo)	430
5-Chloro-2-methyl	1-(<i>p</i> -Sulfophenyl)-3-phenyl-4-(5-chloro-2-methylphenylazo)	430
1-(<i>p</i> -Sulfophenyl)-3-(2-furyl)	1-(<i>p</i> -Sulfophenyl)-3-(2-furyl)-4-phenylazo	430
2-Nitro	1-(<i>p</i> -Sulfophenyl)-3-(2-furyl)-4-(<i>o</i> -nitrophenylazo)	430
4-Nitro	1-(<i>p</i> -Sulfophenyl)-3-(2-furyl)-4-(<i>p</i> -nitrophenylazo)	430
2,5-Dichloro	1-(<i>p</i> -Sulfophenyl)-3-(2-furyl)-4-(2,5-dichlorophenylazo)	430
4-Chloro-2-methyl	1-(<i>p</i> -Sulfophenyl)-3-(2-furyl)-4-(4-chloro-2-methylphenylazo)	430
5-Chloro-2-methyl	1-(<i>p</i> -Sulfophenyl)-3-(2-furyl)-4-(5-chloro-2-methylphenylazo)	430

Note. References 177-480 are on pp. 130-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

TABLE X—Continued
A. 5-*P*-grazolones—Continued

Heterocyclic Compound, Substituent(s) in	Product (Yield, %), Substituent(s) in	References
		
1-(<i>m</i> -Sulfamylphenyl)-3-methyl	1-(<i>m</i> -Sulfamylphenyl)-3-methyl-4-(2-hydroxy-4-sulfo-1-naphthylazo)	433
1-Diphenylmethyl-3-methyl 1-(2-Naphthyl)-3-methyl	1-(<i>m</i> -Sulfamylphenyl)-3-methyl-4-(2-hydroxy-4-sulfo-6-nitro-1-naphthylazo)	433
1-(2-Anthraquinonyl)-3-methyl	1-Diphenylmethyl-3-methyl-4-(<i>p</i> -tolylazo)	434
	1-(2-Naphthyl)-3-methyl-4-(2-anthraquinonylazo) (quant.)	250
	1-(2-Anthraquinonyl)-3-methyl-4-phenylazo	250
	1-(2-Anthraquinonyl)-3-methyl-4-(α -naphthylazo)	250
	1-(2-Anthraquinonyl)-3-methyl-4-(β -naphthylazo)	250
	1-(2-Anthraquinonyl)-3-methyl-4-(2-anthraquinonylazo)	250
1-(2-Benzothiazolyl)-3-methyl	1-(2-Benzothiazolyl)-3-methyl-4-phenylazo	435
	1-(2-Benzothiazolyl)-3-methyl-4-(<i>p</i> -sulfophenylazo)	435

II Miscellaneous Heterocyclic Compounds

Heterocyclic Reactant	Substituent(s) in Aniline*	Product (Yield, %)	Reference
1-Methyl-3-hydroxy-5-pyrazolone imide	4-Methoxy	1-Methyl-3-hydroxy-4-(<i>p</i> -methoxyphenylazo)-5-pyrazolone imide (25)	411
3-(<i>p</i> -Tolyl)-5-pyrazolone imide	—	3-(<i>p</i> -Tolyl)-4-phenylazo-5-pyrazolone imide	318
1-Phenyl-3-methyl-5-pyrazolone imide	—	1-Phenyl-3-methyl-4-phenylazo-5-pyrazolone imide (50)	437, 439
4-Sulfo	—	1-Phenyl-3-methyl-4-(<i>p</i> -sulphophenylazo)-5-pyrazolone imide	435
β-Naphthylamine	—	1-Phenyl-3-methyl-4-(β-naphthylazo)-5-pyrazolone imide	439
1-(<i>o</i> -Tolyl)-3-methyl-5-pyrazolone imide	—	1-(<i>o</i> -Tolyl)-3-methyl-4-phenylazo-5-pyrazolone imide	440
1-Phenyl-3-methyl-5-thiopyrazolone	—	1-Phenyl-3-methyl-4-phenylazo-5-thiopyrazolone	441, 442
1-Phenyl-5-methyl-3-pyrazolone	—	1-Phenyl-4-phenylazo-5-methyl-3-pyrazolone	443, 444
1-(<i>o</i> -Tolyl)-5-methyl-3-pyrazolone	—	1-(<i>o</i> -Tolyl)-4-phenylazo-5-methyl-3-pyrazolone	444
1-(<i>p</i> -Tolyl)-5-methyl-3-pyrazolone	—	1-(<i>p</i> -Tolyl)-4-phenylazo-5-methyl-3-pyrazolone	444
1-(<i>p</i> -Bromophenyl)-5-methyl-3-pyrazolone	—	1-(<i>p</i> -Bromophenyl)-4-phenylazo-5-methyl-3-pyrazolone	445
1-(<i>o</i> -Carboxyphenyl)-5-methyl-3-pyrazolone	—	1-(<i>o</i> -Carboxyphenyl)-4-phenylazo-5-methyl-3-pyrazolone	446
Pyrazolidine-3,5-dione	4-Methyl	4-(<i>p</i> -Tolylazo)pyrazolidine-3,5-dione	404
1-Phenylpyrazolidine-3,5-dione	—	1-Phenyl-4-phenylazopyrazolidine-3,5-dione	447
1-Phenyl-4-ethylpyrazolidine-3,5-dione	4-Methyl	1-Phenyl-4-(<i>p</i> -tolylazo)pyrazolidine-3,5-dione	448
	—	1-Phenyl-4-ethyl-4-phenylazopyrazolidine-3,5-dione	449

Note: References 177-180 are on pp. 138-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

TABLE X—Continued
B. Miscellaneous Heterocyclic Compounds—Continued

Heterocyclic Reactant	Substituent(s) in Aniline*	Product (Yield, %)	References
1- <i>p</i> -Tolylpyrazolidine-3,5-dione	—	1-(<i>p</i> -Tolyl)-4-phenylazopyrazolidine-3,5-dione	450
3-Methyl-5-isoxazolone	—	3-Methyl-4-phenylazo-5-isoxazolone (quant.)	451, 227, 452
	2-Methyl	3-Methyl-4-(<i>o</i> -tolylazo)-5-isoxazolone	227
	4-Methyl	3-Methyl-4-(<i>p</i> -tolylazo)-5-isoxazolone	227
	2-Methoxy	3-Methyl-4-(<i>o</i> -anisylazo)-5-isoxazolone	227
	α -Naphthylamine	3-Methyl-4-(α -naphthylazo)-5-isoxazolone	227
	β -Naphthylamine	3-Methyl-4-(β -naphthylazo)-5-isoxazolone	227
	—	3-Phenyl-4-phenylazo-5-isoxazolone	453
3-Phenyl-5-isoxazolone	—	3-(<i>m</i> -Tolyl)-4-phenylazo-5-isoxazolone	454
3-(<i>m</i> -Tolyl)-5-isoxazolone	—	3-(<i>p</i> -Tolyl)-4-phenylazo-5-isoxazolone	454
3-(<i>p</i> -Tolyl)-5-isoxazolone	—	3-(<i>m</i> -Chlorophenyl)-4-(<i>p</i> -nitrophenylazo)-5-isoxazolone	455
3-(<i>m</i> -Chlorophenyl)-5-isoxazolone	4-Nitro	3-(<i>m</i> -Nitrophenyl)-4-(<i>p</i> -nitrophenylazo)-5-isoxazolone	455
3-(<i>m</i> -Nitrophenyl)-5-isoxazolone	4-Nitro	3-Anilino-4-phenylazo-5-isoxazolone	450
3-Anilino-5-isoxazolone	—	3-Methyl-4-phenylazo-5-iminoisoxazole	90
3-Methyl-5-iminoisoxazole	—	3-Benzyl-5-(<i>p</i> -nitrophenylazo)-4-imidazolone	457
2-Benzyl-4-imidazolone	4-Nitro	4-(<i>p</i> -Tolylazo)-1,2,3-triazol-5-one	458
1,2,3-Triazol-5-one	4-Methyl	1-Carboxymethyl-4-(<i>p</i> -tolylazo)-1,2,3-triazol-5-one	458
1-Carboxymethyl-1,2,3-triazol-5-one	4-Methyl		
1-Phenyl-1,2,3-triazol-5-one	—	1-Phenyl-4-phenylazo-1,2,3-triazol-5-one	459
1-Acetylbenzaldehyde-1,2,3-triazol-5-one	4-Methyl	1-Acetylbenzaldehyde-4-(<i>p</i> -tolylazo)-1,2,3-triazol-5-one	460
1-Acetylglycinbenzaldehyde-1,2,3-triazol-5-one	4-Methyl	1-Acetylglycinbenzaldehyde-4-(<i>p</i> -tolylazo)-1,2,3-triazol-5-one	460
Barbituric acid	—	5-Oxobarbituric acid phenylhydrazone (quant.)	461
	2-Nitro	5-Oxobarbituric acid <i>o</i> -nitrophenylhydrazone	461

TABLE X—Continued
B. Miscellaneous Heterocyclic Compounds—Continued

Heterocyclic Reactant Homophthalimide	Substituent(s) in Aniline*	Product (Yield, %)	References
	—	α -Phenylazohomophthalimide	470, 471, 472
	2-Methyl	α -(<i>o</i> -Tolylazo)homophthalimide	472
	3-Methyl	α -(<i>m</i> -Tolylazo)homophthalimide	472
	4-Methyl	α -(<i>p</i> -Tolylazo)homophthalimide	472
	2-Chloro	α -(<i>o</i> -Chlorophenylazo)homophthalimide	472
	2-Nitro	α -(<i>o</i> -Nitrophenylazo)homophthalimide	472
	4-Nitro	α -(<i>p</i> -Nitrophenylazo)homophthalimide	472
	2-Carboxy	α -(<i>o</i> -Carboxyphenylazo)homophthalimide	472
	3-Carboxy	α -(<i>m</i> -Carboxyphenylazo)homophthalimide	472
	4-Sulfo	α -(<i>p</i> -Sulfophenylazo)homophthalimide	473
	2,4-Dimethyl	α -(2,4-Dimethylphenylazo)homophthalimide	472
	4-Methyl-2-nitro	α -(4-Methyl-2-nitrophenylazo)homophthalimide	472
	4-Methyl-3-nitro	α -(4-Methyl-3-nitrophenylazo)homophthalimide	472
	α -Naphthylamine	α -(1-Naphthylazo)homophthalimide	472
	β -Naphthylamine	α -(2-Naphthylazo)homophthalimide	472
	4-Sulfo-1-naphthylamine	α -(4-Sulfo-1-naphthylazo)homophthalimide	473
	6,8-Disulfo-2-naphthylamine	α -(6,8-Disulfo-2-naphthylazo)homophthalimide	473
	2-Hydroxy-4-sulfo-1-naphthylamine	α -(2-Hydroxy-4-sulfo-1-naphthylazo)homophthalimide	473
	Benidine	α, α' -(4,4'-Biphenylenedisazo)bis(homophthalimide)	472
	3,3'-Dimethylbenzidine	α, α' -(3,3'-Dimethyl-4,4'-biphenylenedisazo)bis(homophthalimide)	472
	3,3'-Dimethoxybenzidine	α, α' -(3,3'-Dimethoxy-4,4'-biphenylenedisazo)bis(homophthalimide)	472

N-Phenylhomophthalimide			
4-Hydroxycoumarin		α -Phenylazo-N-phenylhomophthalimide	474
		3-Phenylazo-4-hydroxycoumarin (91)	475
4-Methyl		3-(<i>p</i> -Tolylazo)-4-hydroxycoumarin (88)	475
4-Nitro		3-(<i>p</i> -Nitrophenylazo)-4-hydroxycoumarin (75)	475
4-Sulfo		3-(<i>p</i> -Sulfamylphenylazo)-4-hydroxycoumarin (10)	475
4-Sulfamyl		3-(<i>p</i> -Sulfamylphenylazo)-4-hydroxycoumarin (50)	475
3-Nitro		1-Methyl-3-(<i>m</i> -nitrophenylazo)-4-hydroxycarbostryl	476a
		γ -Ketoglutaconic anhydride phenylhydrazone (87)	475a
2-Methyl		γ -Ketoglutaconic anhydride <i>o</i> -tolylhydrazone (57)	475a
4-Methyl		γ -Ketoglutaconic anhydride <i>p</i> -tolylhydrazone (79)	475a
2-Methoxy		γ -Ketoglutaconic anhydride <i>o</i> -anisylhydrazone (56)	475a
4-Dimethylamino		γ -Ketoglutaconic anhydride <i>p</i> -dimethylaminophenyl- hydrazone (84)	475a
2-Carboxy		γ -Ketoglutaconic anhydride <i>o</i> -carboxyphenyl- hydrazone (80)	475a
α -Naphthylamine		γ -Ketoglutaconic anhydride α -naphthylhydrazone (86)	475a
β -Naphthylamine		γ -Ketoglutaconic anhydride β -naphthylhydrazone (87)	475a
		γ -Keto- β -methylglutaconic anhydride phenylhydrazone (70)	8b
2-Methoxy		γ -Keto- β -methylglutaconic anhydride <i>o</i> -anisylhydrazone (62)	8b
4-Methoxy		γ -Keto- β -methylglutaconic anhydride <i>p</i> -anisylhydrazone (40)	8b
2-Nitro		γ -Keto- β -methylglutaconic anhydride <i>o</i> -nitrophenyl- hydrazone (64)	8b
4-Dimethylamino		γ -Keto- β -methylglutaconic anhydride <i>p</i> -dimethylamino- phenylhydrazone (72)	8b
4-Diethylamino		γ -Keto- β -methylglutaconic anhydride <i>p</i> -diethylamino- phenylhydrazone (71)	8b

Note: References 177-480 are on pp. 130-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

TABLE X—Continued
B. Miscellaneous Heterocyclic Compounds—Continued

Heterocyclic Reactant	Substituent(s) in Aniline*	Product (Yield, %)	References
β -Methylglutaconic anhydride (Cont.)	4-Sulfo	γ -Keto- β -methylglutaconic anhydride <i>p</i> -sulphophenyl- hydrazone (S5)	Sb
	3-Trifluoromethyl	γ -Keto- β -methylglutaconic anhydride <i>m</i> -trifluoromethyl- phenylhydrazone (S5)	Sb
	2,4-Dinitro	γ -Keto- β -methylglutaconic anhydride 2,4-dinitrophenyl- hydrazone (S9)	Sb
	α -Naphthylamine	γ -Keto- β -methylglutaconic anhydride α -naphthyl- hydrazone (S5)	Sb
	β -Naphthylamine	γ -Keto- β -methylglutaconic anhydride β -naphthyl- hydrazone (S5)	Sb
β -Chloroglutaconic anhydride	—	β -Chloro- γ -ketoglutaconic anhydride phenylhydrazone	476b
β -Carboxyglutaconic anhydride (<i>trans</i> -aconitic anhydride)	—	β -Carboxy- γ -ketoglutaconic anhydride phenylhydrazone (S4)	476c
β -Carbomethoxyglutaconic anhydride	—	β -Carbomethoxy- γ -ketoglutaconic anhydride phenyl- hydrazone (70)	476c
Malonyl- α -aminopyridine	—	3-Phenylazo-4H-pyrido[1,2- <i>a</i>]pyrimidin-4-one (S5)	300b
	4-Carboxy	3-(<i>p</i> -Carboxyphenylazo)-4H-pyrido[1,2- <i>a</i>]pyrimidin-4-one (96)	300b
	4-Carbomethoxy	3-(<i>p</i> -Carbomethoxyphenylazo)-4H-pyrido[1,2- <i>a</i>]- pyrimidin-4-one (70)	300b
	4-Carbethoxy	3-(<i>p</i> -Carbethoxyphenylazo)-4H-pyrido[1,2- <i>a</i>]pyrimidin- 4-one	300b
	4-Sulfo	3-(<i>p</i> -Sulphophenylazo)-4H-pyrido[1,2- <i>a</i>]pyrimidin-4-one (93)	300b

Note: References 177-480 are on pp. 130-142.

* The full name is given when it is awkward to name the arylamine as a derivative of aniline.

TABLE XI
COUPLING OF DIAZONIUM SALTS WITH MISCELLANEOUS COMPOUNDS

Reactant	Substituent in Aniline	Product (Yield, %)	References
Diazomethane	4-Nitro	Chloroformaldehyde <i>p</i> nitrophenylhydrazine* (85)	476d
Acetaldehyde	—	N,N'-Diphenyl-C-phenylazoformazan (20-30)	153, 27
Ketene diethylacetal	—	1-Phenyl-4-ethoxy-6-pyridazine (35)	477
	4-Ethoxy	1- <i>p</i> -Ethoxyphenyl-4 ethoxy-6-pyridazine† (21)	477
	4-Nitro	1- <i>p</i> -Nitrophenyl 4-ethoxy-6-pyridazine (25)	477
	4-Carboethoxy	1- <i>p</i> -Carboethoxyphenyl-4-ethoxy-6-pyridazine (33)	477
Ethyl β aminocrotonate	—	Ethyl α phenylazo-β-aminocrotonate (52)	478
Ethyl β-methylaminocrotonate	—	Ethyl α-phenylazo-β methylaminocrotonate (51)	478
Ethyl β diethylaminocrotonate	—	1-Phenyl-3-diethylamino-3-methyl-4-phenylazo-5-ethoxypyrazoline (75)	479
Bis(phenylsulfinyl)methane	—	Bis(phenylsulfinyl)formaldehyde phenylhydrazine	480
1-(2-Methylpropenyl)piperidine	4-Chloro	Acetone <i>p</i> -chlorophenylhydrazine	130a
	4-Nitro	Acetone <i>p</i> -nitrophenylhydrazine	130a
1-(1-Butenyl)piperidine	4-Methoxy	1,2-Butanedione 2- <i>p</i> -anisylhydrazine (53)	130a
	4-Chloro	1,2-Butanedione 2- <i>p</i> chlorophenylhydrazine (65)	130a
	4-Nitro	1,2-Butanedione 2- <i>p</i> -nitrophenylhydrazine (41)	130a
N,N-Diethylstyrylamine	4-Methoxy	Phenylglyoxal β- <i>p</i> -anisylhydrazine (76)	130a
	4-Chloro	Phenylglyoxal β- <i>p</i> -chlorophenylhydrazine (90)	130a
	4-Nitro	Phenylglyoxal β <i>p</i> -nitrophenylhydrazine (94)	130a
	4-Carboxy	Phenylglyoxal β- <i>p</i> -carboxyphenylhydrazine (89)	130a
	4-Nitro	Acetophenone <i>p</i> -nitrophenylhydrazine (87)	130a
1-(β-Methylstyryl)piperidine	4-Carboxy	Acetophenone <i>p</i> carboxyphenylhydrazine (95)	130a
	2,4-Dinitro	Acetophenone 2,4-dinitrophenylhydrazine (97)	130a

Note: References 177-480 are on pp. 136-142.

* The reaction was run in methanol saturated with lithium chloride.

† Nineteen per cent of N,N'-di-*p*-ethoxyphenyl-C-carboethoxyformazan was also formed.

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CHAPTER 2

THE JAPP-KLINGEMANN REACTION

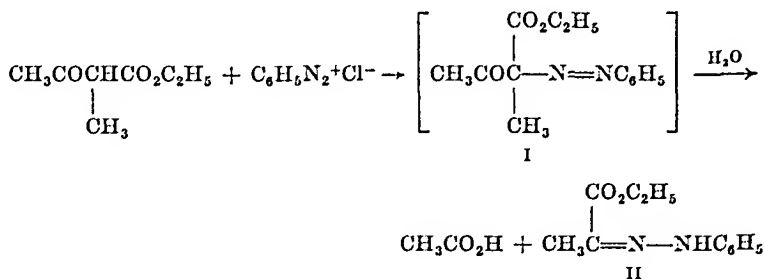
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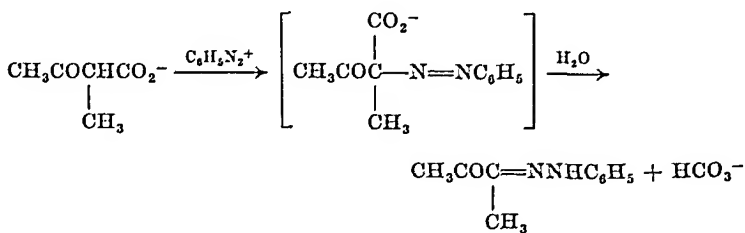
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INTRODUCTION

In an attempt to prepare the azo ester I by coupling benzenediazonium chloride with ethyl 2-methylacetoacetate, Japp and Klingemann¹ obtained a product which was soon recognized¹⁻⁴ as the phenylhydrazone of ethyl pyruvate (II). It thus appeared that the acetyl group had been dis-



placed; actually the coupling product I was unstable under the conditions of its formation, undergoing hydrolytic scission of the acetyl group and rearrangement of the azo structure. A year later the same authors discovered that, if the substituted acetoacetic ester was saponified and the coupling carried out on the sodium salt, the carboxylate function, rather than the acetyl group, was lost and the product isolated was the phenylhydrazone of biacetyl.^{4,5}



In later years the reaction has been extended to other systems containing activated methinyl groups. The process can be generalized as shown in the following equation, in which x and y are electron-withdrawing groups.

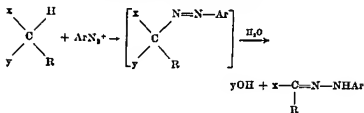
¹ Japp and Klingemann, *Ber.*, 20, 2942 (1887).

² Japp and Klingemann, *Ber.*, 20, 3284 (1887).

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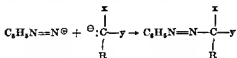
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MECHANISM

As is apparent from the above equations the Japp-Klingemann reaction is a special case of the coupling of diazonium salts with aliphatic compounds (see Chapter I), distinguished by the fact that the coupling product ordinarily undergoes solvolysis as rapidly, or almost as rapidly, as it is formed. It resembles very closely the nitrosation and cleavage of active methinyl compounds discussed in an earlier volume of this series.⁶ The first step undoubtedly occurs by the same mechanism as the similar coupling with an active methylene compound (for a discussion see p. 6), and is probably best represented as a direct union of the anion of the active methinyl compound and the diazonium cation, which are shown in the accompanying equation as the forms carrying full unit charges on the atoms that unite in the process.



Much of the early concern⁷⁻⁹ about the mechanism of such couplings dealt with the question of the participation of the enolic forms of the active methinyl compounds and with the status of O-azo compounds as possible intermediates (p. 4). Although the mechanism just shown is probably an accurate representation of the coupling of mono- β -keto esters, there can be little doubt but that O-azo compounds are sometimes first formed from di- β -keto esters and triketones. Thus tribenzoylmethane yields a coupling product that generates an azo dye upon treatment with β -naphthol and undoubtedly is the derivative of the enol.¹⁰

⁶ Touster, in Adams, *Organic Reactions*, Vol. 7, Chapter 6, John Wiley & Sons, 1953.

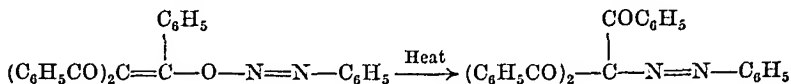
⁷ Dimroth and Hartmann, *Ber.*, 41, 4012 (1908).

⁸ Dimroth, *Ber.*, 40, 2404 (1907).

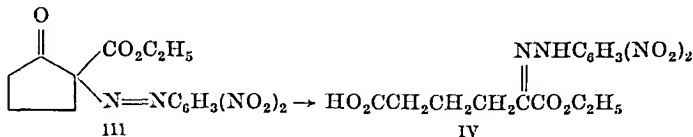
⁹ Dimroth and Hartmann, *Ber.*, 40, 4460 (1907).

¹⁰ Dimroth, Leuchth, and Friedemann, *Ber.*, 50, 1834 (1917).

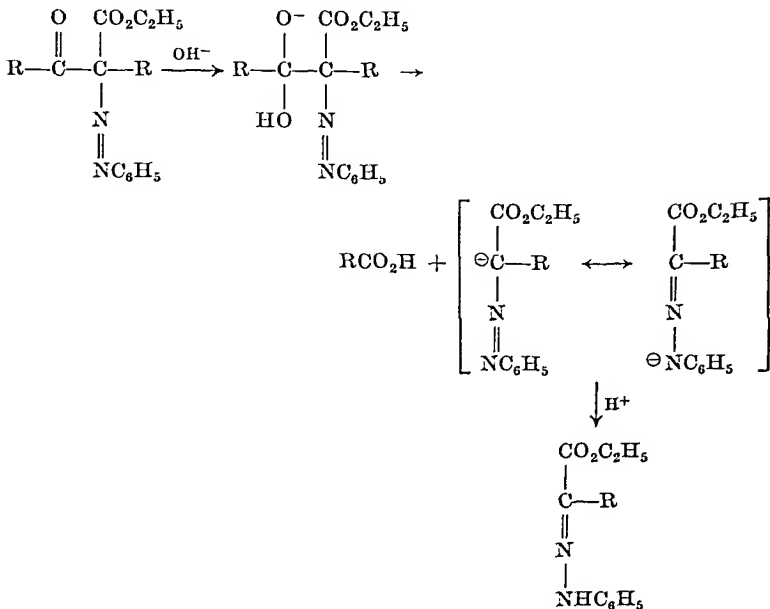
When it is heated to its melting point it changes to an isomer that does not have this property and must be the C-azo compound.



The cleavage step is closely similar to the scission of triacylmethanes and of nitroso derivatives of monosubstituted active methylene compounds.⁷ The cleavage is favored by increasing alkalinity of the solution; for example the azo compound III can be obtained from the diazonium salt prepared from 2,4-dinitroaniline and ethyl cyclopentanone-2-carboxylate by coupling in acetic acid solution, but it is rapidly cleaved by aqueous base, yielding IV.¹¹ In analogy with the base-catalyzed



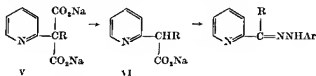
cleavage of nitroso esters⁶ the second step of the Japp-Klingemann reaction can be represented as shown. In the decomposition of the



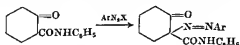
¹¹ Linstead and Wang, *J. Chem. Soc.*, 1937, 807.

product obtained by coupling with a salt of a keto acid, the resonating anion which gives rise to the phenylhydrazone probably results from the loss of carbon dioxide from the carboxylate anion.

Support for the above interpretation of the Japp-Klingemann process can be found in the isolation of many intermediate azo compounds,^{7,11-14} although not all attempts to obtain these intermediates have been successful.¹² That the coupling with salts of β -keto acids and malonic acids does not proceed by a direct displacement of the carboxyl group is indicated by the observation that malonate salts of the type V react much more slowly than their decarboxylation products VI.¹⁵ Thus it appears likely that the malonate salt V undergoes decarboxylation before it reacts with the diazonium salt

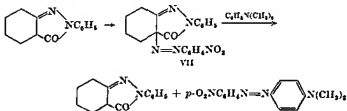


Azo derivatives of cyclohexanone-2-carboxanilide are relatively stable and can be isolated from coupling reactions of the anilide.¹¹ However,



some of the monoaryldiazo of cyclohexanedione was formed along with the azoanilide, presumably as a result of hydrolysis followed by decarboxylation

The phenylpyrazolone obtained from ethyl cyclohexanone-2-carboxylate couples with diazotized *p*-nitroaniline to give the unusually interesting azo derivative VII. Although quite unstable, VII does not undergo the



¹¹ Favrel, *Bull. soc. chim. France*, [4], 47, 1290 (1930).

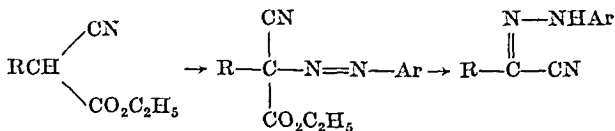
¹² Favrel, *Compt. rend.*, 169, 335 (1927).

¹³ Kalb, Schweitzer, Zellner, and Berthold, *Ber.*, 59, 1860 (1926).

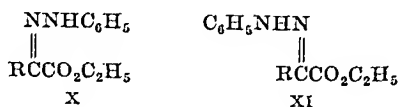
¹⁴ Frank and Phillips, *J. Am. Chem. Soc.*, 71, 2804 (1949).

Bülöw and Hailer applied the Japp-Klingemann reaction to the ethyl esters of several diacylacetic acids.¹⁸ From ethyl propionylacetoacetate they isolated the phenylhydrazone corresponding to cleavage of the propionyl group. The product from ethyl benzoylacetoacetate contained the benzoyl group (loss of acetyl) and that from ethyl phenacetylacetoacetate contained the phenacetyl group (loss of acetyl). It was concluded that in such cleavages the acyl group corresponding to the weaker acid is liberated the more readily (the corrected acidity constants,²² $10^5 K_a$, of the acids concerned are: propionic acid, 1.33; acetic acid, 1.75; phenylacetic acid, 4.88; benzoic acid, 6.27). In a study of the cleavage of unsymmetrical 1,3-diketones of the type $\text{RCOCH}_2\text{COR}'$, Hauser, Swamer, and Ringler²³ found a correlation of the relative yields of the acids RCO_2H and $\text{R}'\text{CO}_2\text{H}$ with the rates of saponification of the ethyl esters of these acids, although the relationship did not hold well with purely aliphatic compounds. On this basis the acetyl group would be expected, contrary to observation, to undergo cleavage in either ethyl benzoylacetoacetate or ethyl propionylacetoacetate (the rate constants, $10^4 k$, for the alkaline hydrolysis of the ethyl esters of the acids are:²⁴ $\text{C}_6\text{H}_5\text{CO}_2\text{C}_2\text{H}_5$, 5.50; $\text{CH}_3\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$, 35.5; $\text{CH}_3\text{CO}_2\text{C}_2\text{H}_5$, 69.5).

In the cleavage of substituted cyanoacetic esters during the second stage of the Japp-Klingemann reaction, saponification and decarboxylation invariably occur leading to the phenylhydrazones of α -ketonitriles. Apparently no instance of the scission of the nitrile group has been recorded.



Perhaps one reason why more precise information is lacking on the direction of cleavage of azodiketones in the Japp-Klingemann reaction is that the arylhydrazones produced in the process usually are capable of existing in geometrically isomeric forms (e.g., X and XI). Both isomers often are produced, and it may be economical to subject the crude



²² Ingold, *Structure and Mechanism in Organic Chemistry*, p. 734, Cornell University Press, Ithaca, N. Y., 1953.

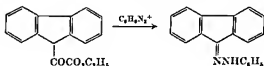
²³ Hauser, Swamer, and Ringler, *J. Am. Chem. Soc.*, **70**, 4023 (1948).

²⁴ Hammett, *Physical Organic Chemistry*, p. 121, McGraw-Hill Book Co., New York, 1940.

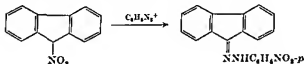
material to the next reaction in a sequence, with purification at a later stage, rather than to isolate the pure arylhydrazone. As a result, yields of the arylhydrazones often are not reported

SCOPE AND APPLICATION

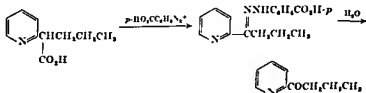
The first requirement for the occurrence of the Japp-Klingemann reaction is the presence of a hydrogen atom of sufficient activity to permit the coupling with the diazonium salt. Although normally two or three electron-withdrawing groups, such as carbonyl, carbethoxyl, cyano, etc., are present in the molecule, only one such group is required if other labilizing influences are operative upon the hydrogen atom concerned. For example, 9-ethoxalylfluorene reacts in the typical fashion.²⁵ A



particularly interesting reaction is that of 9-nitrofluorene;²⁶ in the coupling with diazotized aniline the displaced nitro group appears in the para position of the phenylhydrazine residue of the product.



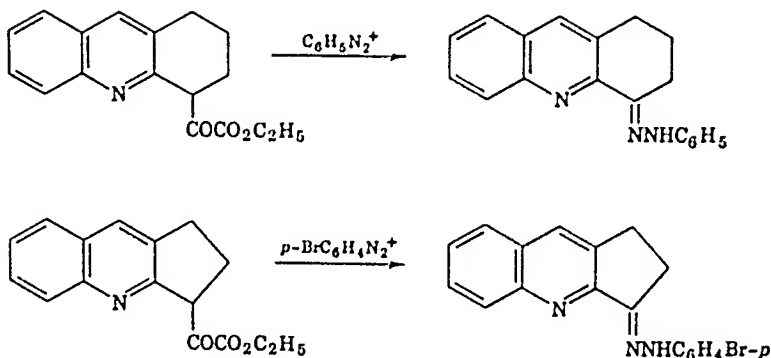
A methinyl group in the α -position of a pyridine compound also is reactive enough to participate in the Japp-Klingemann process if one additional activating group is present. For example, 2-*n*-butylpyridine has been prepared in good yield from 2-(2'-pyridyl)pentanoic acid by the process shown.¹⁵ A somewhat similar reaction is that of 1-ethoxalyl-1,2,3,4-tetrahydroacridine and the analogous cyclopenteno derivative.²⁷



²⁵ Kuhn and Levy, *Ber.*, **61**, 2240 (1928).

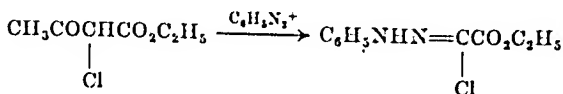
²⁶ Ponzio, *Gazz. chim. ital.*, **42**, (II), 55 (1912).

²⁷ Boreche and Manteuffel, *Ann.*, **534**, 56 (1936).

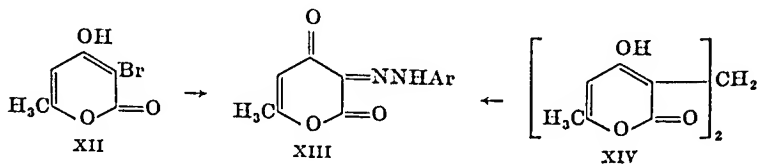


In contrast with 9-nitrofluorene, α -nitropropionic acid retains the nitro group in the reaction. Decarboxylation takes place to yield the phenylhydrazone, $\text{CH}_3\text{C}(\text{NO}_2)=\text{NNHC}_6\text{H}_5$, identical with the product obtained from nitroethane and benzenediazonium chloride.²⁸

Esters of a great variety of monosubstituted acetoacetic acids have been subjected to the reaction. Chlorine and bromine atoms may serve as the third substituent on the methinyl carbon. These halogen atoms are not removed during the reaction but appear in the products, which are phenylhydrazones of unusual structure, as shown in the equation.^{29,30}



One exception to the statement that halogen is not removed is the coupling of 3-bromotriacetic lactone (XII), which furnishes the same arylhydrazone XIII as that obtained from triacetic lactone itself.^{30a} Methylene bis(triacetic lactone) (XIV) on coupling also yields the arylhydrazone XIII.



Alkyl-substituted acetoacetic esters are more commonly encountered. The products from such esters are readily reduced and hydrolyzed, and

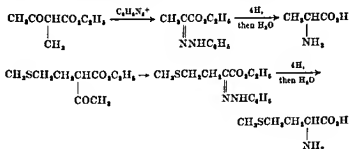
²⁸ Steinkopf and Supan, *Ber.*, **43**, 3239 (1910).

²⁹ Favrel, *Compt. rend.*, **134**, 1312 (1902).

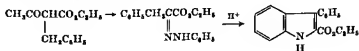
³⁰ Favrel, *Bull. soc. chim. France*, [3], **31**, 150 (1904).

^{30a} Wiley and Jarboe, *J. Am. Chem. Soc.*, **78**, 624 (1956).

this method of synthesis of α -amino acids has been employed extensively. Examples are the syntheses of alanine^{3,31-34} and methionine.³⁵



The phenylhydrazones from the Japp-Klingemann reaction on simply substituted acetoacetic esters also have been used extensively in the synthesis of indoles. The Fischer cyclization converts them to esters of substituted indole-2-carboxylic acids. The preparation of ethyl 3-phenylindole-2-carboxylate is illustrative.³⁶



Substituents in the benzene ring of the indole may be introduced through the use of a substituted benzenediazonium salt in the coupling. Diazonium salts from 2- and 4-substituted anilines can give only one product in a simple Fischer cyclization, but two different indoles may be obtained from a *m*-substituted aniline,³⁷ and consequently these have been employed infrequently. Examples of the products obtained from 2- and 4-substituted anilines are shown.^{38,39}

³¹ Feofilaktov, *Compt rend acad. sci. U.R.S.S.*, 24, 755 (1939) [*C. A.*, 34, 1971 (1940)].

³² Feofilaktov and others, *Bull. acad. sci. U.R.S.S. Classe sci. chim.*, 1940, 259 [*C. A.*, 35, 3606 (1941)].

³³ Bamberger, *Ber.*, 25, 3647 (1892).

³⁴ Feofilaktov and Zaitseva, *J. Gen. Chem. U.S.S.R.*, 10, 258 (1940) [*C. A.*, 34, 7293 (1940)].

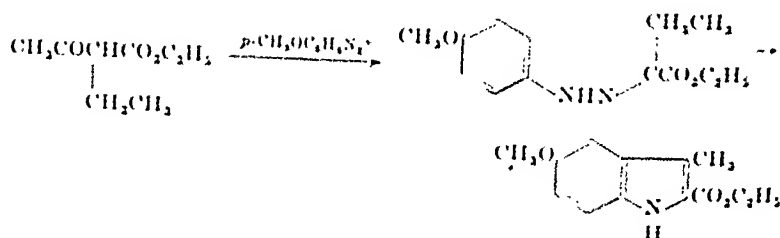
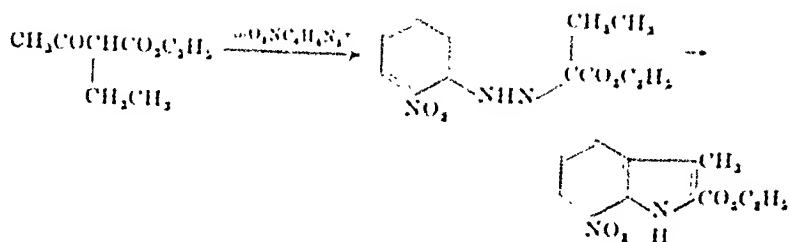
³⁵ Feofilaktov and Ivanova, *J. Gen. Chem. U.S.S.R.*, 21, 1694 (1951) [*C. A.*, 46, 3965 (1952)].

³⁶ Manake, Perkin, and Robinson, *J. Chem. Soc.*, 1927, 1.

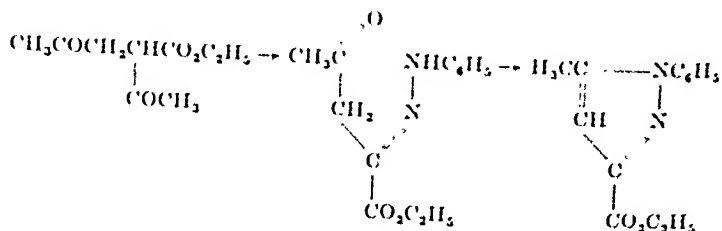
³⁷ Koelsch, *J. Org. Chem.*, 8, 295 (1943).

³⁸ Hughes, Lions, and Ritchie, *J. Proc. Roy. Soc. N. S. Wales*, 72, 209 (1938) [*C. A.*, 33, 6827 (1939)].

³⁹ Hughes and others, *J. Proc. Roy. Soc. N. S. Wales*, 71, 475 (1937) [*C. A.*, 33, 567 (1939)].

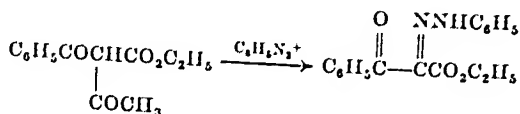


If the substituent in the acetoacetic ester has a carbonyl group attached to the first carbon atom, the phenylhydrazone from the Japp-Klingemann reaction will readily cyclize to a pyrazole. Acetonyl¹⁰ and phenacyl¹¹



groups, which may bear additional substituents, have been employed in this way.

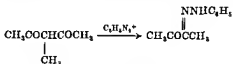
Acyl derivatives of acetoacetic ester also may be employed. The products are monophenylhydrazones of α,β -diketo esters. Thus ethyl benzoylacetoacetate reacts as shown.¹²



¹⁰ Bischler, *Ber.*, 26, 1881 (1893).

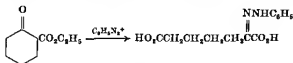
¹¹ Bischler, *Ber.*, 25, 3143 (1892).

Probably because they have been less readily available than acetoacetic esters, 1,3-diketones have not been extensively employed in the Japp-Klingemann reaction. Among those which have been examined are α -chloro-,⁴² α -methyl-⁴³ and α -ethyl-acetylacetone.⁴² The products are monophenylhydrazones of 1,2-diketones, as illustrated for the methyl derivative. The same products are available from the substituted β -keto

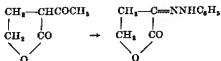


esters, provided the ester group is saponified before the coupling is performed (p 144). Such monophenylhydrazones have been prepared from several substituted acetoacetic esters.

When the Japp-Klingemann reaction is applied to a cyclic β -keto ester, the ring is opened in the second stage of the process. The reaction of ethyl cyclohexanone-2-carboxylate is illustrative.^{11,44} Cyclopentanone



derivatives undergo similar ring opening. The products from both series have been employed in the synthesis of amino acids and indoles. The ring opened may be that of a lactone, as in acetobutyrolactone, which yields the phenylhydrazone of ketobutyrolactone.⁴⁵ This product also



has found use in the synthesis of amino acids.^{46,47} Alternatively the ring opened may be that of a lactam, as in the elegant synthesis of tryptamine

⁴² Dieckmann and Platz, *Ber.*, **38**, 2936 (1905)

⁴³ Favrel, *Bull. soc. chim. France*, [3], **27**, 336 (1902), *Compt. rend.*, **132**, 41 (1901)

⁴⁴ Feofilaktov and Yvanov, *J. Gen. Chem. U.S.S.R.*, **13**, 457 (1943) [*C. A.*, **38**, 3255 (1944)].

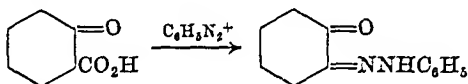
⁴⁵ Haradence and Lyons, *J. Proc. Roy. Soc. N.S. Wales*, **72**, 221 (1938) [*C. A.*, **33**, 6836 (1939)].

⁴⁶ Feofilaktov and Onishchenko, *J. Gen. Chem. U.S.S.R.*, **9**, 314 (1939) [*C. A.*, **34**, 378 (1940)]

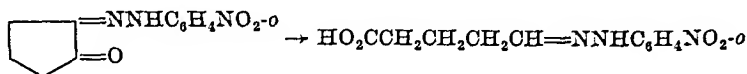
⁴⁷ Snyder, Andreen, Cannon, and Peters, *J. Am. Chem. Soc.*, **64**, 2082 (1942)

and serotonin (5-hydroxytryptamine) based on the coupling with a salt of α -carboxy- α -valerolactone and a Fischer cyclization of the products.^{47a}

As in the reactions of acyclic β -keto esters, the reaction takes the decarboxylation course if the ester is saponified before the coupling. Thus a monophenylhydrazone of cyclohexane-1,2-dione is obtained from ethyl cyclohexanone-2-carboxylate.¹¹

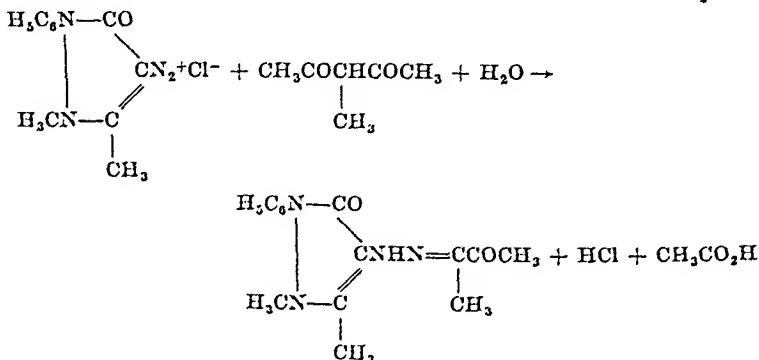


Such compounds may serve as sources of derivatives of ω -aldehyde acids. When the *o*-nitrophenylhydrazone obtained from cyclopentanone-2-carboxylic acid was allowed to stand in aqueous alcoholic potassium hydroxide for five days it was converted to the *o*-nitrophenylhydrazone of δ -formylbutyric acid in about 35% yield.¹¹



Monosubstituted cyanoacetic esters couple readily. When the products are hydrolyzed, decarboxylation ensues leading to hydrazones of α -keto nitriles. Substituted malonic esters yield phenylhydrazones of α -keto acids, identical to those which can be obtained from similarly substituted acetoacetic esters.

The diazonium salts used in the reaction include those derived from aniline and its simple substitution products, polysubstituted anilines, benzidine and substituted benzidines, and even antipyrine. The diazonium salt related to the last substance has been coupled with 3-methylpentane-2,4-dione⁴⁸ to give the hydrazone shown in the equation.



^{47a} Abramovitch and Shapiro, *Chemistry & Industry*, 1955, 1255.

⁴⁸ Morgan and Reilly, *J. Chem. Soc.*, 103, 808 (1913).

It might be expected that diazonium salts in which electron-withdrawing groups are located in ortho or para positions, so that they accentuate the positive character of the diazonium cation, would be most active in the coupling. In couplings with 2-pyridylacetic acid, diazotized *p*-aminobenzoic acid gave the best results, and diazotized *p*-nitroaniline and sulfanilic acid were superior, both with regard to the yield and the purity of the products, to diazotized aniline.¹⁵ Although few experiments have been carried out with a single active methinyl compound and a variety of diazonium salts in the Japp-Klingemann reaction under identical conditions, the yields from substituted anilines appear to run higher than those from aniline. It is possible that substituents such as the nitro and carboxyl groups may give rise to higher melting and less soluble products, leading to easier isolation as well as to more complete reaction.

If the arylamino portion of a Japp-Klingemann product is to be removed, as in a reduction to an α -amino acid (pp 152-153), the diazonium salt should be selected not only on the basis of the probable yield in the coupling but also with consideration of the character of the second product in the further reaction. For example, if a diazotized aminobenzoic acid were used in a coupling carried out as part of a sequence to an α -amino acid, the difficulty of separating this product from the regenerated aminobenzoic acid might outweigh any advantage gained in the coupling.

In the preparation of arylhydrazones to be employed in the synthesis of indoles and pyrazoles the choice of the diazonium salt is dictated by the substituents desired in the final product.

EXPERIMENTAL CONDITIONS

Most of the reactions have been run in aqueous medium at about 0°. Occasionally ethanol has been added to increase the solubility.⁴⁹ In the coupling of 1-ethoxalyl-1,2,3,4-tetrahydroacridine (p. 151) the medium was pyridine diluted with the water in which the diazonium salt was prepared.²⁷ The aqueous solutions usually are buffered with sodium acetate in reactions in which an acyl group is to be cleaved.^{20,50} Stronger bases have been used, however. In the conversion of ethyl cyclopentanone-2-carboxylate to the phenylhydrazone of ethyl hydrogen α -keto-adipate, Manske and Robinson⁵¹ employed potassium hydroxide; for the preparation of the similar product from diazotized *m*-aminobenzoic acid,

⁴⁹ Lyons and Spruon, *J. Proc. Roy. Soc. N. S. Wales*, 66, 171 (1932) [*C. A.*, 27, 291 (1933)].

⁵⁰ Favrel and Chrz, *Bull. soc. chim. France*, (4), 37, 1238 (1925).

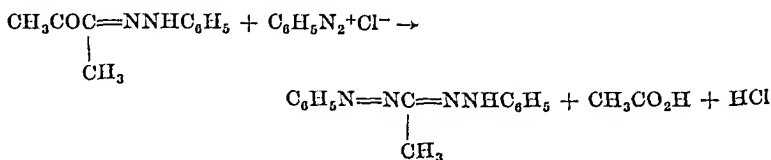
⁵¹ Manske and Robinson, *J. Chem. Soc.*, 1927, 240

Koelsch³⁷ preferred to carry out the coupling in acid solution and to convert the azo compound so obtained to the substituted hydrazone by a two-minute treatment with boiling 7% aqueous sodium carbonate. Other couplings also have been found to occur under either acid or basic conditions,^{8,43,52} and even sodium ethoxide has been used as the base.⁵³

If the cleavage of the acyl group from a β -keto ester is desired, the basic solution of the ester should be treated with the diazonium salt immediately.⁵⁴ If such basic solutions are allowed to stand at 0° for periods up to twenty-four hours before the treatment with the diazonium salt, the ester group is removed and the product obtained is a derivative of a 1,2-diketone.^{11,55,56}

The time required for the Japp-Klingemann process varies, with the activity of the methinyl group, from a few seconds to as much as four days.¹⁵ When aqueous solutions are employed the products often separate, and the mixture can be stirred until no further change occurs. The azo compounds, sometimes encountered as intermediates (p. 147), are much more deeply colored (usually red) than the arylhydrazones. Accordingly, a color change sometimes furnishes a useful guide to the course of the reaction.

Most of the reactions have been run with equivalent amounts of the methinyl component and the diazonium salt. The use of excess diazonium salt may result in the loss of some of the product by conversion to the formazyl, as shown in the equation.^{33,57} This appears to be the only



serious side reaction in the Japp-Klingemann process, aside from the alternative cleavage of keto esters (above). Another disadvantage to the use of an excess of the diazonium salt is the formation of colored materials and tars as a result of its decomposition when the reaction mixture is allowed to warm.

The products from the Japp-Klingemann reaction usually have been

⁵² Findlay and Dougherty, *J. Org. Chem.*, **13**, 560 (1948).

⁵³ Feofilaktov, *J. Gen. Chem. U.S.S.R.*, **17**, 993 (1947) [*C. A.*, **42**, 4537 (1948)].

⁵⁴ Jackson and Manske, *J. Am. Chem. Soc.*, **52**, 5029 (1930).

⁵⁵ Manske, *Can. J. Research*, **4**, 591 (1931).

⁵⁶ Lions, *J. Proc. Roy. Soc. N. S. Wales*, **66**, 516 (1932) [*C. A.*, **27**, 2954 (1933)].

⁵⁷ Walker, *J. Chem. Soc.*, **123**, 2775 (1923).

recrystallized from ethanol or benzene; 80% acetic acid has been employed in some instances.⁵⁴

EXPERIMENTAL PROCEDURES

Ethyl Pyruvate *o*-Nitrophenylhydrazone.⁵⁴ To an ice-cold solution of 20.5 g. (0.14 mole) of ethyl 2-methylacetoacetate in 150 ml. of ethanol is added 51 ml of 50% aqueous potassium hydroxide. This mixture is then diluted with 300 ml of ice water, and the cold diazonium salt solution, prepared from 20.0 g. (0.14 mole) of *o*-nitroaniline, 60 ml. of concentrated hydrochloric acid, 90 ml of water, and 10.5 g. of sodium nitrite, is rapidly run in with stirring. Stirring is continued for five minutes, at the end of which time the separated ethyl pyruvate *o*-nitrophenylhydrazone is collected by filtration. It melts at 106°, after recrystallization from ethanol. The yield is 30.0 g (83%).

1,2-Cyclohexanedione Monophenylhydrazone.⁵⁶ To an ice-cold solution of 36.0 g. (0.21 mole) of ethyl cyclohexanone-2-carboxylate in 40 ml. of ethanol is added an ice-cold solution of 12.0 g. of potassium hydroxide in 60 ml. of water. The reaction mixture is held at 0° for twenty-four hours and then diluted with 1 l. of ice water. A benzene-diazonium chloride solution is prepared from 18.6 g. (0.2 mole) of aniline, 50 ml. of concentrated hydrochloric acid in 100 ml. of water, and 13.8 g. of sodium nitrite. The cold diazonium solution is then added to the first solution with vigorous stirring and continued cooling in ice, followed immediately by the addition of 30.0 g of sodium acetate. Carbon dioxide is seen to evolve, and the reaction is allowed to continue at 0° until the gas evolution ceases. The solid product which separates is 1,2-cyclohexanedione monophenylhydrazone. It is collected by filtration and recrystallized from ethanol. It melts at 185–186°. The yield is almost quantitative.

TABULAR SURVEY OF THE JAPP-KLINGEMANN REACTION

The following list of Japp-Klingemann reactions includes many examples in which the products were further modified, so that yields are not available. The list is based on a literature survey to January 1, 1956, but because of the difficulties of locating scattered instances of the reaction in the literature, especially when the products are chiefly of interest as intermediates in further reactions, it probably does not include

⁵⁴ Feofilaktov and Vinogradova, *Compt rend acad sci U.R.S.S.*, **24**, 759 (1939) [*C. A.*, **34**, 1971 (1940)]

all recorded applications of the Japp-Klingemann reaction. For convenience the reactions in which an acyl group is cleaved are listed separately (section A) from those accompanied by decarboxylation (section B). Accordingly, some compounds will be found in both sections. Section A is subdivided as follows:

I. Derivatives of nitropropionic, formylpropionic, and haloacetoacetic acids.

II. Monosubstituted acetoacetic esters.

III. Acylacetoacetic esters.

IV. Acylcyanoacetic esters.

V. Cyclic compounds.

VI. 1,3-Dicarbonyl compounds.

VII. Miscellaneous compounds.

Section B is subdivided as follows:

VIII. Acetoacetic acid derivatives.

IX. Cyanoacetic acid derivatives.

X. Malonic acid derivatives.


XI. Miscellaneous reactions.

A. Reactions in Which an Acyl Group Is Cleaved

TABLE I

DERIVATIVES OF FORMYLPROPIONIC AND HALOACETOACETIC ACIDS

(The group lost in the cleavage is *italic*.)

Substance	Substituent in  N ₂ ⁺ or [Other Diazonium Ion]	Yield, %	References	Conversion Product
CH ₃ CHCO ₂ C ₂ H ₅ CHO	—	—	16	—
CH ₃ COCHCO ₂ CH ₃ Cl	— — 2-CH ₃ 4-CH ₃	— — — —	30 59 30 30	— — — —
CH ₃ COCHCO ₂ C ₂ H ₅ Cl	— —* 2-CH ₃ 4-CH ₃ * 4-Br*	— — — — —	29, 30 59 29, 30 29, 30 60	— — — — —
	[Certain benzidine derivatives]			
CH ₃ COCHCONHC ₂ H ₅ Cl	4-CH ₃ 3-CH ₃ , 4-CH ₃ 3-CH ₃ , 5-CH ₃ [α-C ₁₀ H ₇ N ₂ ⁺] [β-C ₁₀ H ₇ N ₂ ⁺]	80 — — — —	61 61 61 61 61	— — — — —
CH ₃ COCHCO ₂ C ₁₀ H ₁₉ †‡ Br	— 4-Br 4-CH ₃	— — —	62 62 62	— — —

Note: References 59-118 are on pp. 177-178.

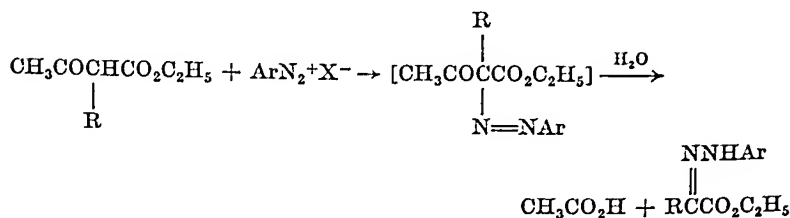
* These reagents have also been coupled with ethyl α-bromoacetoacetate, ref. 60.


† The (—)-menthyl ester.

‡ Certain reactions of the ethyl ester are entered under ethyl α-chloroacetoacetate.

TABLE II

MONOSUBSTITUTED ACETOACETIC ESTERS IN THE REACTION:




Substituent R in $\text{CH}_3\text{COCHCO}_2\text{C}_2\text{H}_5$	Substituent in  N_2^+ or [Other Diazonium Ion]	Yield, %	References	Conversion Product
CH_3	—	38	5, 31-34	Amino acid
	2- CH_3	—	1, 5	—
	4- CH_3	—	1, 5	—
	2- NO_2	83	38	Indole
	3- NO_2	—	12	—
		84	63	—
	4- NO_2	78	63	—
	4-Br	—	39	Indole
	4- OCH_3	—	39	Indole
	2- OC_2H_5	—	39	Indole
	4- OC_2H_5	—	39	Indole
	4- $\text{CO}_2\text{C}_2\text{H}_5$	—	39	Indole
	3- OCH_3 , 4- OCH_3	73	49	Indole
	$[\alpha\text{-C}_{10}\text{H}_7\text{N}_2^+]$	—	39	Indole
	$[\beta\text{-C}_{10}\text{H}_7\text{N}_2^+]$	—	39	Indole
C_2H_5	—	—	1, 5	—
	2- NO_2	90	38	Indole
	3- NO_2	—	12	—
	4-Br	—	39	—
	4- OCH_3	—	39	Indole
	4- OC_2H_5	—	39	Indole
	4- $\text{CO}_2\text{C}_2\text{H}_5$	—	39	Indole
	3- OCH_3 , 4- OCH_3	70	49	Indole
	$[\alpha\text{-C}_{10}\text{H}_7\text{N}_2^+]$	—	39	Indole
	$[\beta\text{-C}_{10}\text{H}_7\text{N}_2^+]$	—	39	Indole
$\text{CH}_3\text{SCH}_2\text{CH}_2$	—	73	35, 117	Amino acid
$(\text{C}_2\text{H}_5)_2\text{NCH}_2\text{CH}_2$	—	76	64	Indole
$n\text{-C}_3\text{H}_7$	—	35	65	Amino acid
	4- CH_3	43	65	Amino acid
	2- NO_2	97	38	Indole
$i\text{-C}_3\text{H}_7$	—	55	66	Amino acid

Note: References 59-118 are on pp. 177-178.

TABLE II—Continued

MONOSUBSTITUTED ACETOACETIC ESTERS IN THE REACTION:

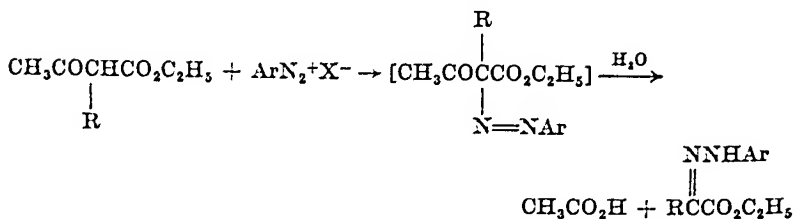
$\text{CH}_3\text{COCH}(\text{R})\text{CO}_2\text{C}_2\text{H}_5 + \text{ArN}_2^+\text{X}^- \rightarrow [\text{CH}_3\text{C}(\text{R})\text{C}(\text{O})\text{CO}_2\text{C}_2\text{H}_5] \xrightarrow{\text{H}_2\text{O}}$ $\text{CH}_3\text{CO}_2\text{H} + \text{RCCO}_2\text{C}_2\text{H}_5$				
Substituent R in $\text{CH}_3\text{COCH}(\text{R})\text{CO}_2\text{C}_2\text{H}_5$	Substituent in  N ₂ ⁺ or [Other Diazonium Ion]	Yield, %	References	Conversion Product
CH ₃ COCH ₃	—	—	40	Pyrazole
C ₂ H ₅ O ₂ CCH ₂ CH ₃	4-NO ₂ *	—	67	Pyrazole
	—	74	113	—
	2-CH ₃	88	113	—
	3-CH ₃	34	113	—
	2-Cl	60	113	—
	3-Cl	72	113	—
	4-Cl	81	113	—
	2-CO ₂ H	90	113	—
	4-SO ₃ H	95	113	—
	4-NO ₂	87	113	—
	(α-C ₁₀ H ₇ N ₃)	47	113	—
	(β-C ₁₀ H ₇ N ₃)	33	113	—
NCCH ₂ CH ₃	—	98	112, 113	Indole
	4-NO ₂	98	113	—
C ₄ H ₉ O ₂ CCH ₂ CH ₃	—	—	68, 69	Indole
	2-Cl	—	52	—
	3-Cl	—	52	—
	4-Cl	—	52	—
	2-CH ₃	—	111	Amino acid
	2-OCH ₃	—	52	Indole
	3-OCH ₃	—	52	Indole
	4-OCH ₃	—	52	Indole
C ₆ H ₅ OCH ₂ CH ₂ CH ₃	—	15	70	Indole
C ₆ H ₅ O ₂ CCH ₂ CH ₃	—	Good	71	Indole
 NHCO ₂ C ₂ H ₅				

Note: References 59-118 are on pp. 177-178.

* The azo compound was isolated; upon standing or upon treatment with aqueous alkali, followed by acidification, it underwent loss of the acetyl group and cyclization to the pyrazole.

TABLE II—Continued

MONOSUBSTITUTED ACETOACETIC ESTERS IN THE REACTION:




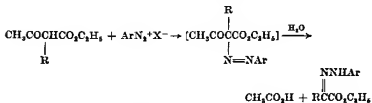



Substituent R in $\text{CH}_3\text{COCHCO}_2\text{C}_2\text{H}_5$	Substituent in  N_2^+ or [Other Diazonium Ion]	Yield, %	References	Conversion Product
$n\text{-C}_4\text{H}_9$	—	65	72	Amino acid
	2-NO ₂	—	38	Indole
	4-Br	—	39	Indole
	4-OCH ₃	—	39	Indole
	2-OC ₂ H ₅	—	39	Indole
	4-OC ₂ H ₅	—	39	Indole
	4-CO ₂ C ₂ H ₅	—	39	Indole
	[$\alpha\text{-C}_{10}\text{H}_7\text{N}_2^+$]	—	39	Indole
(CH ₃) ₂ CHCH ₂	—	72	31, 32, 73	Amino acid
CH ₃ CH ₂ CH(CH ₃)	—	63	31, 32, 73	Amino acid
CH ₃ COCH(CO ₂ C ₂ H ₅)	—	Quant.	74, 75, 76	Pyrazole
	4-CH ₃	Quant.	77	Pyrazole
	4-CH ₃ CONH†	—	78	Pyrazole
	4-($p\text{-H}_2\text{NC}_6\text{H}_4$)†	—	78	Pyrazole
	4-($p\text{-CH}_3\text{CONHC}_6\text{H}_4$)†	—	78	Pyrazole
	[$\beta\text{-C}_{10}\text{H}_7\text{N}_2^+$]	—	77	Pyrazole
C ₆ H ₅ CH ₂	—	68	31, 32, 79	Amino acid
	—	Quant.	80	Azoformal- doxime
	2-NO ₂	90	38	Indole
	4-Br	—	39	Indole
	4-OCH ₃	—	39	Indole
	2-OC ₂ H ₅	—	39	Indole
	4-OC ₂ H ₅	—	39	Indole
	4-CO ₂ C ₂ H ₅	—	39	Indole
	3-OCH ₃ , 4-OCH ₃	70	49	Indole
	[$\alpha\text{-C}_{10}\text{H}_7\text{N}_2^+$]	—	39	Indole
	[$\beta\text{-C}_{10}\text{H}_7\text{N}_2^+$]	—	39	Indole
4-CH ₃ OC ₆ H ₄ CH ₂	—	75	81	Amino acid

TABLE II—Continued

MONOSUBSTITUTED ACETOACETIC ESTERS IN THE REACTION:

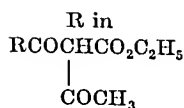
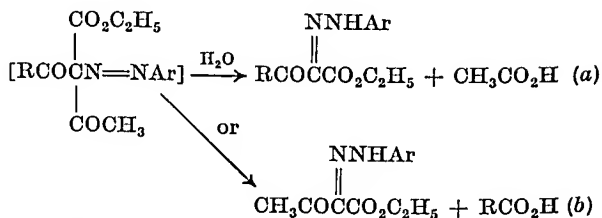
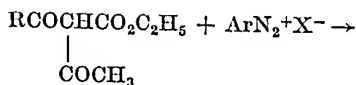


Substituent R in $\text{CH}_3\text{COCHCO}_2\text{C}_2\text{H}_5$	Substituent in  N ₃ ⁺ or [Other Diazonium Ion]	Yield, %	References	Conversion Product
	—	70	82	Indole
	—	50	82	Indole
$\text{C}_6\text{H}_5\text{COCH}_3$	—	—	41	Pyrazole
	2-CH ₃	—	40	Pyrazole
	4-CH ₃	—	40	Pyrazole
$\text{C}_6\text{H}_5\text{COCH}(\text{C}_6\text{H}_5)$	—	—	40	Pyrazole

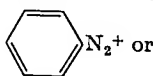
Note: References 59–118 are on pp. 177–178.

TABLE III

ACYLACETOACETIC ESTERS IN THE REACTION:

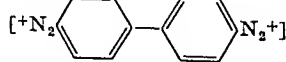


Substituent in



[Other Diazonium Ion]

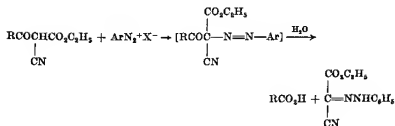
Yield, %	Refer- ences	Conversion Product
—	18	—
—	18	—
—	18	—
—	83	—
—	18	—
—	18	—
—	18	—
—	18	—
—	18	—
—	18	—
—	18	—
—	18	—
—	18	—

 CH_3 CH_3CH_2^* $\text{C}_2\text{H}_5\text{O}^\dagger$ $\text{C}_2\text{H}_5\text{OCO}^\dagger$ $\text{C}_6\text{H}_5^\dagger$ 2-CO₂H2-CH₃4-NO₂2-CO₂H3-O₂NC₆H₄†4-O₂NC₆H₄†C₆H₅CH₂CO†2-CO₂H

Note: References 59-118 are on pp. 177-178.

* Reaction course *b*.† Reaction course *a*.

TABLE IV
ACYLCYANOACETIC ESTERS IN THE REACTION:




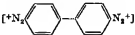
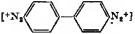
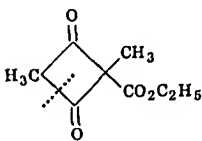
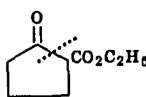
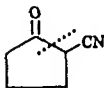
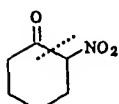
R in Ester	Substituent in	Yield, %	Refer- ences	Conversion Product
	[Other Diazonium Ion]			
CH ₃	 N ₂ ⁺ or	—	20, 21	—
	[Other Diazonium Ion]	—	20, 21	—
CH ₃ CH ₂ (CH ₂) ₃ CH		—	20	—
	—	—	20, 21	—
	—	—	20, 21	—
(CH ₃) ₂ CHCH ₂ C ₆ H ₅		—	20	—
	—	—	20, 21	—
	—	—	20, 21	—

TABLE V
CYCLIC COMPOUNDS IN RING-OPENING REACTIONS*

Cyclic Compound†	Substituent in	Yield, %	References	Conversion Product
	[Other Diazonium Ion]			
	4-NO ₂	Good‡	84	—
	—	96	11, 51, 53, 85, 114	Indole
	2-NO ₂	—	11	Indole
	4-NO ₂	—	11, 14	Indole
	3-CO ₂ H	70	37	Indole
	4-I	65	14	Indole
	4-OCH ₃	71	86	Indole
	3-I, 4-I, 5-I	95	14	—
	3-I, 4-OCH ₃ , 5-I	88	14	—
	[α-C ₁₀ H ₇ N ₂ ⁺]	94	53	Indole
	—	—	87	—
	—	—	88	—

Note: References 59-118 are on pp. 177-178.

* See p. 155.

† The bond broken in the ring opening is indicated by the dotted line.

‡ The reported product is
$$\text{O}_2\text{NC}_6\text{H}_4\text{N}=\text{N}-\overset{\text{CH}_3}{\underset{\text{CO}_2\text{H}}{\text{C}}}-\text{CO}-\overset{\text{CH}_3}{\text{CH}}\text{CO}_2\text{C}_2\text{H}_5.$$

TABLE V—Continued

CYCLIC COMPOUNDS IN RING-OPENING REACTIONS*

Substituent in



Cyclic Compound†	[Other Diazonium Ion]	Yield, %	References	Conversion Product
	—	—	44	Amino acid
—	—	97	115, 118	Indole
—‡	—	87	11, 54	—
2-NO ₂	—	—	38	Indole
4-NO ₂	—	—	11	—
3-OCH ₃ , 4-OCH ₃	—	90	49	Indole
	—	89	89, 116	—

Note: References 59–118 are on pp. 177–178.

* See p. 155.

† The bond broken in the ring opening is indicated by the dotted line.

‡ Methyl cyclohexanone-2-carboxylate was also coupled.



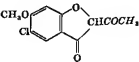
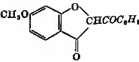
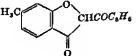
TABLE VI
1,3-DICARBONYL COMPOUNDS
(The group that is lost is italic.)

Carbonyl Compound	Substituent in [Other Diazonium Ion]	Yield, %	Refer- ences	Con- version Product
$\text{CH}_3\text{COCHCOCH}_3$ Cl	— —	— 69	42 90	— —
$\text{CH}_3\text{COCHCOCO}_2\text{C}_2\text{H}_5$ Cl	—	—	91	—
$\text{CH}_3\text{COCHCOCH}_3$ CH ₃	— 2-CH ₃ 4-CH ₃ 4-NO ₂	— — — —	43 43 43 13	— — — —
	$[\text{N}_2\text{C}_6\text{H}_4\text{—C}_6\text{H}_4\text{N}_2^+]$	—	43	—
	$[\text{N}_2\text{C}_6\text{H}_3(\text{CH}_3)\text{—C}_6\text{H}_3(\text{CH}_3)\text{N}_2^+]$	—	43	—
	$\begin{array}{c} \text{H}_3\text{C}_6\text{N—CO} \\ \quad \diagdown \\ \quad \text{CN}_2^+ \\ \quad \diagup \\ \text{H}_3\text{CN—C} \\ \\ \text{CH}_3 \end{array}$	—	48	—
$\text{CH}_3\text{COCHCOCH}_3$ CH ₂ CH ₃	— 2-CH ₃ 4-CH ₃ 4-NO ₂ 4-Cl 4-Br	— — — — — —	43 43 43 13 13 13	— — — — — —
	$[\text{N}_2\text{C}_6\text{H}_4\text{—C}_6\text{H}_4\text{N}_2^+]$	—	43	—

Note: References 59–118 are on pp. 177–178.

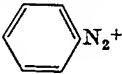
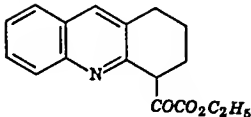
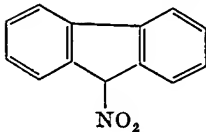
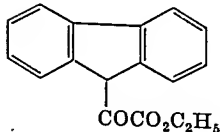
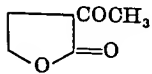
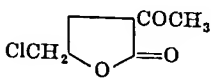
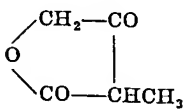
TABLE VI—Continued

1,3-DICARBONYL COMPOUNDS
(The group that is lost is italic.)

Carbonyl Compound	Substituent in  N ₂ ⁺ or [Other Diazonium Ion]	Yield, %	Refer- ences	Con- version Product
$\text{CH}_3\text{COCHCOCH}_3$ $\text{CH}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	—	90 (as acid)	113	—
	2-CH ₃	72 (as acid)	113	—
	3-CH ₃	85 (as acid)	113	—
	4-CH ₃	81 (as acid)	113	—
	4-NO ₂	85 (as acid)	113	—
$\text{C}_6\text{H}_5\text{COCHCHO}$ C_6H_5	—	—	92, 93	—
	4-Br	—	9	—
	4-NO ₂	—	8	—
	—	—	94	—
	—	—	19	—
	—	—	19	—
	—	—	19	—

Note: References 59–118 are on pp. 177–178.

TABLE VII
MISCELLANEOUS COMPOUNDS

Starting Material	Substituent in 	Yield, %	References	Conversion Product
	—*	—	27	—
	4-OCH ₃ *	—	27	—
	4-Br*	—	27	—
	—†	—	26	—
	—‡	—	95	—
	4-NO ₂ ‡	—	25	—
	—	90-96	45, 46, 47	Amino acid
	—	83	96, 97	Amino acid
	—	—	98	—

Note: References 59-118 are on pp. 177-178.

* The reaction was run in pyridine solution.


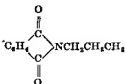
† The nitro group eliminated from the 9 position of fluorene apparently attacked the coupling product, since the *p*-nitro-phenylhydrazone of fluorenone was isolated.

‡ The ethoxalyl group was eliminated.

B. Reactions Accompanied by Decarboxylation

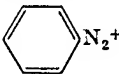
TABLE VIII

ACETOACETIC ACID DERIVATIVES

R in $\begin{array}{c} \text{R in} \\ \text{RCHCO}_2\text{H} \\ \\ \text{COCH}_3 \end{array}$	Substituent in 	Yield, %	References	Conversion Product
CH ₃	—	Quant.	4, 5, 33	—
C ₆ H ₅	—	—	4, 5	—
KO ₂ CCH ₂ CH ₃	—	80	99	—
C ₆ H ₅ CH ₂	—	86	36	Indole
	3-NO ₂	80	36	—
	2-OCH ₃ , 5-OCH ₃	80	36	—
	3-OCH ₃ , 4-OCH ₃	Quant.	49	—
C ₆ H ₅ COCH ₃	—	—	40	Pyrazole
	—	86	36	Indole
	3-OCH ₃	85	36	Indole
	3-Cl	—	36	—

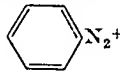
Note: References 59-118 are on pp. 177-178.

TABLE IX
CYANOACETIC ACID DERIVATIVES

R in RCHCO_2H $\text{C}\equiv\text{N}$	Substituent in 	Yield, %	References	Conversion Product
CH_3	—	—	100, 101	—
	2- CH_3	25	100, 101	—
	4- CH_3	28	100, 101	—
C_2H_5	—	31	100, 101	—
	2- CH_3	25	100, 101	—
	4- CH_3	15	100, 101, 102	—
	4-Cl	Quant.	102	—
C_6H_5	—	—	102	—
$\text{C}_6\text{H}_5\text{CH}_2$	—	30	58, 103	Amino acid
	—	Quant.	102	—
	4- CH_3	25	102	—
	4- NO_2	—	102	—




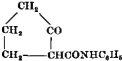



Note: References 59–118 are on pp. 177–178.

TABLE X
MALONIC ACID DERIVATIVES

R in $\text{RCH}(\text{CO}_2\text{H})_2$	Substituent in 	Yield, %	References	Conversion Product
Cl	—	—	59	—
	2- CO_2CH_3	—	59	—
CH_3	—	—	104, 105	—
	4- CH_3	—	104, 105	—
C_2H_5	—	—	104, 105	—
	2- CH_3	—	104, 105	—
$\text{HO}_2\text{CCH}_2\text{CH}_2$	—	49	113	—
$\text{C}_6\text{H}_5\text{CH}_2$	—	—	58, 103	Amino acid
	—	—	80	Azoformaldoxime

Note: References 59–118 are on pp. 177–178.

TABLE XI
MISCELLANEOUS REACTIONS


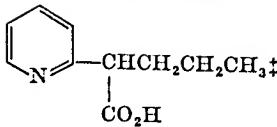
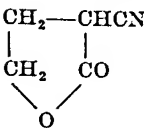
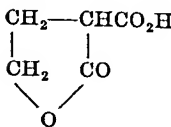
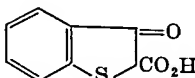
Starting Material	Substituent in  N ₂ ⁺ or [Other Diazonium Ion]	Yield, %	References	Conversion Product
	—	—	28	—
	—	Quant.	11, 56, 106	Indole
	2-NO ₂	—	11	—
	4-NO ₂	—	11	—
	2-NO ₂ [*]	—	11	—
	4-NO ₂ [*]	—	11	—
	—	Quant.	11, 56	Indole
	4-CH ₃	Quant.	56	Indole
	4-NO ₂	—	11	Indole
	[α-C ₁₀ H ₇ N ₂ ⁺]	—	56	Indole
	[β-C ₁₀ H ₇ N ₂ ⁺]	Quant.	56	Indole
	—	—	107	—
	4-CO ₂ C ₂ H ₅	89	108	—

Note: References 59-118 are on pp. 177-178.

* The azo compound was isolated also

† The product was α-C₁₀H₇NNHCOCH(CH₃)=NNHC₂H₅CO₂C₂H₅-(p)

TABLE XI—*Continued*
 MISCELLANEOUS REACTIONS

Starting Material	Substituent in  N ₂ ⁺ or [Other Diazonium Ion]	Yield, %	References	Conversion Product
	4-CO ₂ H	94	15	—
	—	88	109	—
	—	83	46	Amino acid
	—	Quant.	110	—

Note: References 59–118 are on pp. 177–178.

† The product was 2-*n*-butyrylpyridine.

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CHAPTER 3

THE MICHAEL REACTION*

ERNST D. BERGMANN

*Scientific Department, Ministry of Defence,
Tel-Aviv*

DAVID GINSBURG

*Chemistry Department, Israel Institute of
Technology, Haifa*

RAPHAEL PAPPO

*Department of Organic Chemistry, Hebrew University,
Jerusalem*

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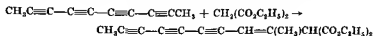
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* This cooperative study was begun when the three authors were working at the Weizmann Institute of Science, Rehovoth.

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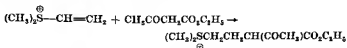
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by this survey, which therefore includes as donors nitriles, nitro compounds, sulfones, and certain hydrocarbons such as cyclopentadiene, indene, and fluorene that contain sufficiently reactive hydrogen atoms. It also includes as acceptor molecules a vinylsulfonium compound²² and certain hydrocarbons of permanent polar character (*finite dipole moment*) such as fulvenes. Another hydrocarbon acceptor is the conjugated tetra-acetylenic compound which adds diethyl sodiomalonate as shown^{22a}



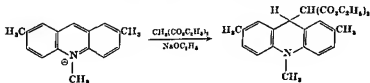
The relatively few Michael condensations in which acetylenic aldehydes, ketones, and esters serve as acceptors are also considered.

The interesting examples of activation of an ethylenic double bond by a neighboring sulfonium group provided by the observation²² that vinyltrimethylsulfonium bromide adds methyl acetoacetate and diethyl malonate in the presence of aqueous sodium hydroxide, according to the following equation,



are good illustrations of the mechanism of the Michael reaction, as set out in the following section.

Unsaturated cyclic quaternary ammonium salts can also act as acceptors in the presence of bases. A recent example is furnished by the 2,7,10-trimethylacridinium halides which react with diethyl malonate in the presence of sodium ethoxide as shown in the accompanying equation.^{22b}



²² Doering and Schreiber, *J. Am. Chem. Soc.*, **77**, 514 (1955).

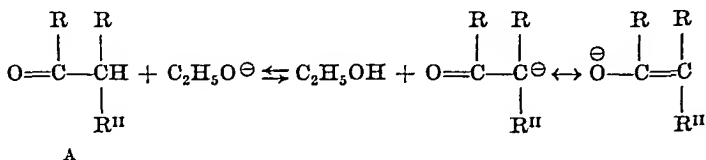
^{22a} Bohlmann, Inhoffen, and Politt, *Ann.*, **604**, 207 (1937).

^{22b} Dumroth and Criegee, *Chem. Ber.*, **90**, 2207 (1957). Other examples are given by Kroehnke and Honig, *Chem. Ber.*, **90**, 2215 (1957); Kroehnke and Vogt, *Ann.*, **600**, 211 (1956), and *Chem. Ber.*, **90**, 2227 (1957). These reactions recall older observations of the reactions of unsaturated cyclic quaternary ammonium pseudo bases with ethyl acetoacetate and with nitroparaffins. Kaufmann, *Chem. Zentr.*, 1912, II, 978. Leonard and Leubner, *J. Am. Chem. Soc.*, **71**, 3405 (1949). Leonard, Leubner, and Burk, *J. Org. Chem.*, **15**, 979 (1950).

MECHANISMS OF THE PROCESSES INVOLVED IN THE MICHAEL REACTION

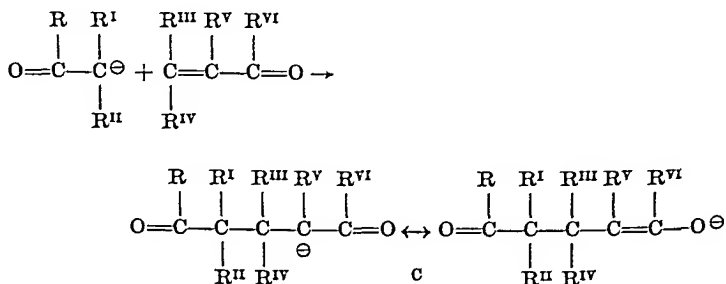
The Normal Reaction

From the nature of the alkaline reagents that cause the Michael condensation to occur, it is logical to suppose that they act by removing the α -hydrogen atom from the donor as a proton. The residual anion is



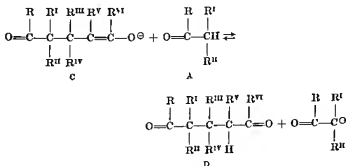
presumably to be viewed as a hybrid of the enolate ion form and the carbanion form, as depicted here, though the subsequent condensation is most readily visualized as involving the carbanion.

The condensation proper occurs when a new bond is formed between the electron-rich carbon of this ion and the most electron-poor carbon of the conjugated system in the acceptor, namely, the β -carbon atom. Where the acceptor has (as shown) carbonyl activation of the α,β double bond, the carbanion product C is a resonance hybrid. It is noteworthy that ability of acceptors to serve in the Michael condensation is enhanced by polarizing substituents (R^{III} , R^{IV} , R^{V}) that stabilize the ions C.



The proton that converts the ionized product (C) into the keto form isolated (D) may come from another donor molecule. This interpretation accounts for the fact that much less than the equivalent amount of basic reagent often suffices to bring about the condensation. Where a full equivalent of base is employed, the proton is supplied by neutralization of the reaction system.

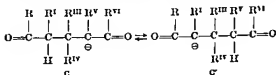
The over-all reaction has, then, the effect of 1,4 addition of the donor (in fragments $\text{O}=\text{C}-\text{C}-$ and $-\text{H}$) to the conjugated system of the acceptor.



The foregoing description obviously does not apply to those condensations, included as Michael reactions in the larger sense, in which the acceptor is an unsaturated hydrocarbon of permanent polar character. Here the product C must be formulated exclusively as a carbanion, and the over-all reaction has the appearance of 1,2 addition of the donor RH (as R— and —H) to the polarized double bond.

The Nature of the Anion of the Adduct

Where R^{II} is hydrogen, the carbanion C may undergo a proton shift. It must be supposed that the anion readily assumes the form C' if this

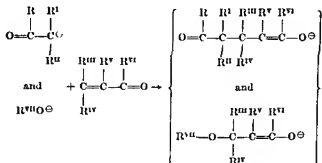


is more stable than C, as may be the case if the substituent R^{I} makes the proton of the group $\text{R}^{\text{I}}\text{CH}$ more highly acidic than that of $\text{R}^{\text{V}}\text{CH}$.

Although on direct isolation the same product is obtained from C and from C', the reactions carried out on the anion may disclose when the change has taken place, as in the following example.²³ The Michael product from ethyl cyanoacetate and ethyl methacrylate (with a full equivalent of base) can be methylated in alcoholic solution with methyl iodide. Upon hydrolysis and decarboxylation, α, α' -dimethylglutaric

A Competitive Side Reaction

Compounds of the type formulated above as acceptors tend to undergo addition reactions with anions in general, e.g., with alkoxide anions, which are frequently used as catalysts in the Michael reaction. In such cases, the catalyst competes with the donor for the acceptor molecule.



Although this possibility should always be borne in mind, it seems that only acceptors in which $\text{R}^{\text{III}} = \text{R}^{\text{IV}} = \text{H}$ (acrylates, acrylonitrile) add alkoxide anions avidly enough to interfere with the Michael reaction. It is preferable with these acceptors to carry out the condensation without solvent or in non-hydroxylic media.²⁷

The Reverse or Retrograde Reaction

The Michael reaction is a reversible process—adducts D can be split into precursors A and B by the same catalysts that effect the condensation.²⁸ A tendency toward such retrogression can be combatted to a degree by using an excess of one of the reactants, this appears to be a case of mass action affecting an equilibrium. Although few quantitative data are available on the position of the equilibrium, it appears that low temperature favors condensation and elevated temperature retrogression.²⁹ Furthermore, retrogression is more likely to occur when the condensation is slow; one of the factors causing slow condensation is the presence of a large number of substituents (R^{III} , R^{IV} , R^{V}) at the α, β double bond of the acceptor molecule (see p. 247). These two effects are exemplified in

²⁷ Koelsch, *J. Am. Chem. Soc.*, **65**, 437 (1943).

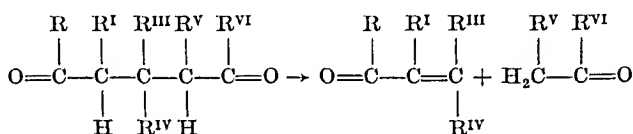
²⁸ Grob and Baumann, *Helv. Chim. Acta*, **38**, 594 (1955).

²⁹ Dornow and Boberg, *Ann.*, **578**, 101 (1952).

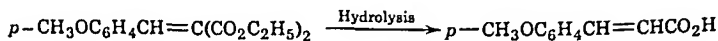
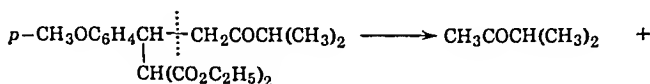
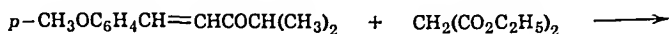
the following table in which the yields of condensation product obtained possibly represent the equilibria attained.

Reaction between Diethyl Malonate and	Yield of Adduct at	
	100°	25°
Ethyl crotonate	65	?
Ethyl cinnamate	35	?
Ethyl β,β -dimethylacrylate	30	70
Ethyl α,β,β -trimethylacrylate	Trace?	?

Whenever at least one of the substituents R^I and R^{II} in the donor is hydrogen, the general formulation of the condensation product acquires



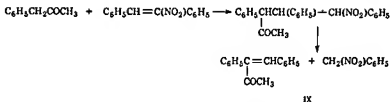
the symmetry of a 1,5-diketopentane with hydrogen atoms in the 2 and 4 positions. With such a structure, retrogression can occur to give fragments different from the starting materials. In this process, the bond broken is the one that was originally α,β in the acceptor; the remainder of this end of the molecule is then isolated as a fragment having $O=C-CH$ ("donor") structure. At the same time, the original donor reappears with $C=C-C=O$ ("acceptor") structure. The combination of condensation and retrogression in such cases has the net effect of transferring an alkylidene substituent from the α -carbon of the original acceptor to the α -carbon of the original donor. Thus, the Michael condensation between phenylacetone and α -nitrostilbene gives, *inter alia*, 3,4-diphenyl-3-buten-2-one (IX),²⁹ and the condensation of isopropyl



p-methoxybenzylidenemethyl ketone with diethyl malonate, when carried out in ethanol as solvent, gives *p*-methoxycinnamic acid.³⁰ (See equations at top of p. 189.)

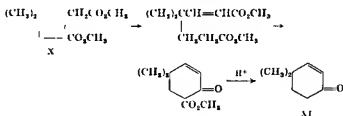
Cleavage formally identical with this can occur in molecules of suitable structure, even though they were not formed by a Michael reaction. The

³⁰ Vorlaender and Knoetzschn, *Ann.*, **294**, 317 (1897), especially p. 334.

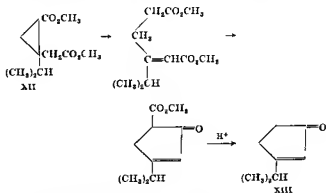


following examples from the chemistry of natural products illustrate cleavages that may be designated retrograde Michael reactions in a formal sense.

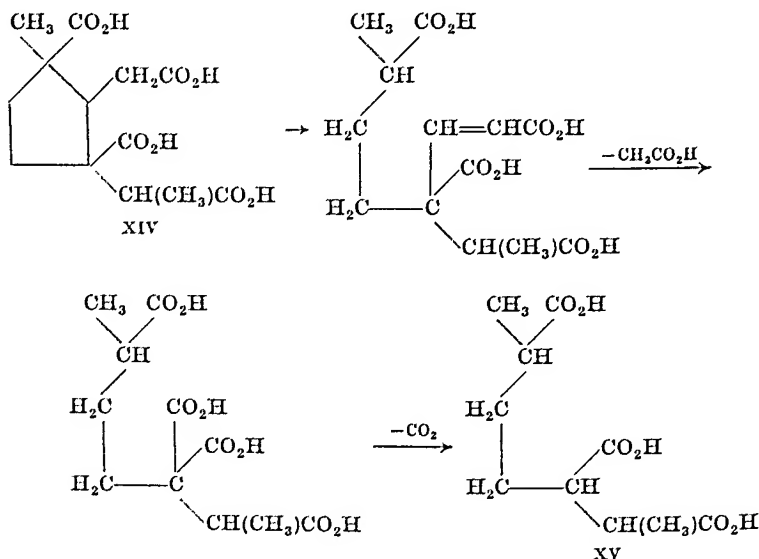
1 Dimethyl caryophyllenate (X) is converted by successive treatments with sodium amide in xylene at 130° and with dilute hydrochloric acid into 4,4-dimethyl-2-cyclohexenone (XI)²¹



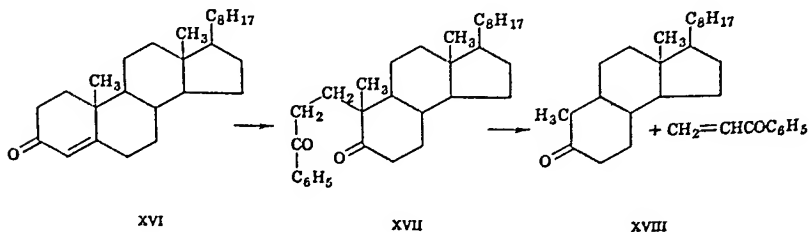
2 Dimethyl α -tanacetonedicarboxylate (XII) is analogously converted into tanacetophorone (XIII).³²

²¹ Eschenmoser and Kuerst, *Experientia*, **7**, 290 (1951).²² Wallace, *Ann.*, 388, 49 (1912).

3. The conversion of santoric acid (XIV) into santoronic acid (heptane-2,3,6-tricarboxylic acid, XV) has been formulated as follows.³³



4. The phenyl ketone XVII, obtained from 4-cholesten-3-one (XVI), is converted (in its intramolecular aldol form) by heating with alkali at 200–240° to XVIII and vinyl phenyl ketone, which decomposes further into formaldehyde and acetophenone.³⁴



5. Pyrolysis of the keto aldehyde XIX gives XX and 2-dodecenal.^{35,36}
 6. Similarly, XXI is converted to 2-methylcyclohexanone and XXII.³⁷

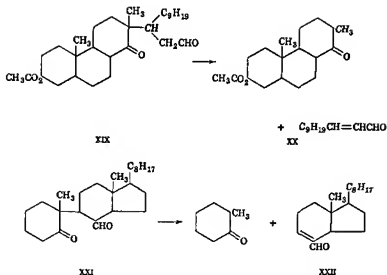
³³ Woodward, Brutsch, and Buer, *J. Am. Chem. Soc.*, **70**, 4216 (1948).

³⁴ Julia, Eschenmoser, Heusser, and Tarköy, *Helv. Chim. Acta*, **36**, 1885 (1953).

³⁵ Achtermann, *Hoppe-Seyler's Z. physiol. Chem.*, **225**, 141 (1934).

³⁶ Laucht, *Hoppe-Seyler's Z. physiol. Chem.*, **237**, 236 (1935).

³⁷ Cornforth, Hunter, and Popjök, *Biochem. J.*, **54**, 599 (1953).



Other retrogressions of this type may take place by heating or under base catalysis ³⁸⁻⁴⁷

The "Abnormal" Michael Condensation

When the Michael condensation product from ethyl β,β -dimethylacrylate and ethyl α -cyanopropionate is methylated (with sodium ethoxide and methyl iodide), the product upon hydrolysis and partial decarboxylation is $\alpha,\alpha',\beta,\beta$ -tetramethylglutaric acid (XXVI) ²³ This carbon skeleton shows that the methylation product before hydrolysis is XXV. In turn, XXV probably can only arise by methylation of XXIV, where the hydrogen atom replaced is doubly activated (enolizable), because it is generally assumed that (singly activated) α -hydrogen atoms like those in XXIII (the alternative possible precursor of XXV) cannot be methylated

²³ Hill, *J Chem Soc*, 1928, 256.

²⁴ Leonard, Simon, and Felley, *J. Am Chem. Soc.*, 73, 807 (1951)

²⁵ Vorlaender, *Ber.*, 33, 3185 (1900).

²⁶ Vorlaender and Koethner, *Ann.*, 345, 158 (1906)

²⁷ Meerwein, *Ber.*, 53, 1829 (1920)

²⁸ Smith and Engelhardt, *J Amer Chem Soc.*, 71, 2676 (1949)

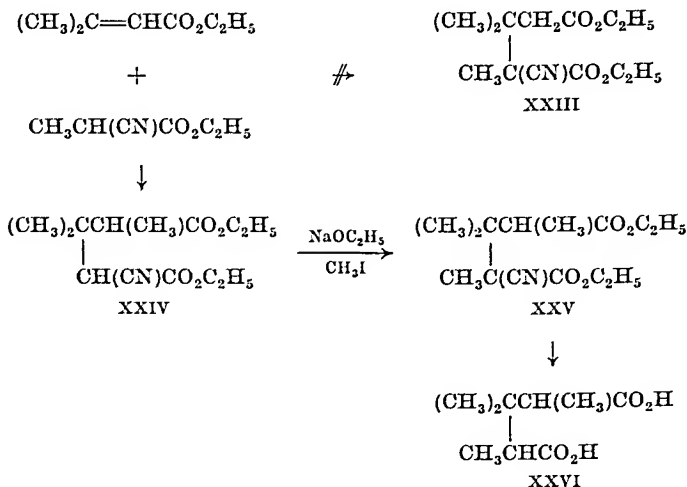
²⁹ Cornelson and Kostanecki, *Ber.*, 29, 240 (1896)

³⁰ Kostanecki and Rossbach, *Ber.*, 29, 1488 (1896).

³¹ Meerwein, *J prakt. Chem.*, [2], 97, 225 (1918)

³² Argon, Viterbo, Duennenberger, Jeger, and Ruzicka, *Helv Chim Acta*, 37, 2306 (1954).

by sodium ethoxide plus methyl iodide.* (Hydrolysis of the primary adduct gives α,β,β -trimethylglutaric acid,⁴⁹ which does not permit differentiation between XXIII and XXIV.) The initial condensation product must therefore be not the expected ("normal") XXIII but the ester XXIV, which is formally the result of adding the donor molecule as the fragments $\text{CH}_3\text{—}$ and $\text{—CH(CN)CO}_2\text{C}_2\text{H}_5$. This is called the "abnormal" Michael reaction; in this and similar cases studied by



Thorpe and co-workers, the products formed were attributed to literal addition of a methyl group as one portion of the donor. "Abnormal" addition of diethyl methylmalonate involves the apparent adding of the fragments $\text{C}_2\text{H}_5\text{OCO—}$ and $\text{—CH(CH}_3\text{)CO}_2\text{C}_2\text{H}_5$.

In some systems, it is observed that the course of the reaction can be varied at will by the amount of condensing agent employed. For example,⁵⁰ diethyl malonate and ethyl crotonate give the normal adduct, triethyl 2-methylpropane-1,1,3-tricarboxylate (XXVII), which, having an enolizable hydrogen atom, can be methylated to triethyl 3-methylbutane-2,2,4-tricarboxylate (XXVIII). The adduct XXVIII is also obtained from ethyl crotonate and diethyl *methylmalonate* in the presence of one-sixth equivalent of sodium ethoxide. If a *full* equivalent of the condensing agent is employed, however, an isomer of XXVIII is formed; this must have the "abnormal" structure XXIX, for it contains an

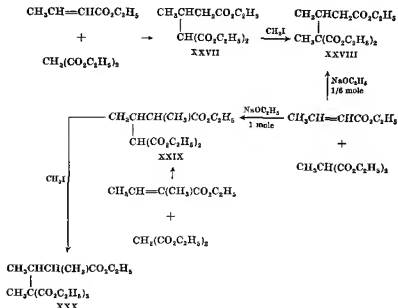
* There are occasional observations to the contrary.**

** Schlenk, Hillemann, and Rodloff, *Ann.*, **487**, 135 (1931).

†† Cf. Michael and Ross, *J. Am. Chem. Soc.*, **53**, 1150 (1931).

‡‡ Michael and Ross, *J. Am. Chem. Soc.*, **52**, 4598 (1930).

enolizable hydrogen atom and can be methylated by sodium ethoxide and methyl iodide to yield XXX. Furthermore, the isomer XXIX can be obtained by the Michael condensation of ethyl tiglate and diethyl malonate, though this synthesis provides valid evidence only if the condensation takes the "normal" course. In contrast to the behavior of

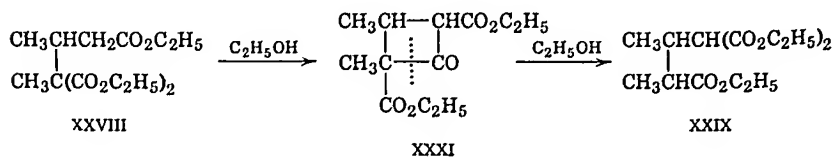


XXIX, when XXVIII is treated again with sodium ethoxide and subsequently methyl iodide, retrogression takes place to ethyl crotonate and diethyl methylmalonate, the latter being further methylated to diethyl dimethylmalonate.

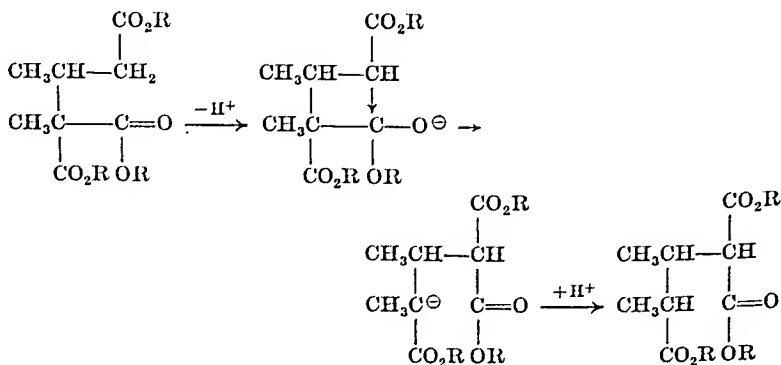
The most widely accepted explanation for the "abnormal" reaction is that of Holden and Lapworth.⁵¹ The primary product of the Michael condensation always has the normal formula (e.g., XXVIII from ethyl crotonate and diethyl methylmalonate), however, it is stable only when small quantities of catalyst are employed. In the presence of larger quantities of catalyst, a Dieckmann condensation is assumed to occur (XXVIII \rightarrow XXXI). This cyclization may be facilitated by the presence of a relatively large number of substituents, which could cause a change

¹² Holden and Lapworth, *J. Chem. Soc.*, 1931, 2368.

in the valence angles, as proposed by Ingold in other cases.^{52,53} The cyclobutanone derivative XXXI in turn is also unstable, particularly as a consequence of the β -keto ester structure; accordingly, it is alcoholized to XXIX, which is the product actually obtained.



A variation of the Holden-Lapworth mechanism proposed later⁵⁴ is based on the assumption that the intermediary product is not a cyclobutanone derivative but the anion of a hemiacetal. This yields, for the reaction of ethyl crotonate with diethyl methylmalonate, the following reaction sequence.



It was emphasized that the C—C linkage connecting the hemiacetal carbon with the CHCO_2R group is "highly polarized" (symbolized \downarrow), but the significance of this statement is not clear. An analogous mechanism was suggested for the abnormal Michael reaction between diethyl methylmalonate and ethyl tetrolate.

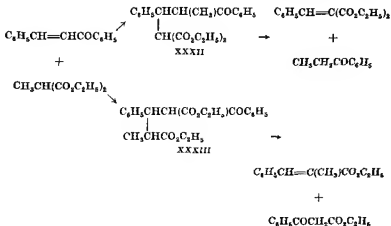
A possible means of distinguishing between the mechanisms of Thorpe and of Holden and Lapworth should be to use an acyl group in the acceptor in place of the carbalkoxy group, i.e., to use an unsaturated ketone rather than an ester. However, an attempt to make the distinction in this way was confounded by instability of the condensation

⁵² Ingold, *J. Chem. Soc.*, 119, 305 (1921).

⁵³ Ingold, *J. Chem. Soc.*, 119, 951 (1921).

⁵⁴ Henecka, *Fortschr. chem. Forsch.*, 1, 685 (1950).

product. Benzylideneacetophenone and diethyl methylmalonate should give XXXII according to Thorpe, and XXXIII according to Holden and Lapworth. In fact, neither of the two compounds was obtained, but instead a mixture of retrogression products, ethyl α -methylcinnamate and ethyl benzoylacetate. These appear to be compatible only with



formula XXXIII, as indicated in the reaction scheme, because if XXXII were formed it would decompose into diethyl benzylidenemalonate and propiophenone.*

Additional evidence on mechanism was sought, with only limited success, by investigations of the condensation of diethyl benzylmalonate with diethyl fumarate,^{56,57} of diethyl benzylmalonate with *trans*-dibenzoyl-ethylene and α -chlorodibenzoyl-ethylene,⁵⁸ of diethyl methylmalonate with ethyl cyclohexene-1-carboxylate and ethyl α -ethylcrotonate,⁵⁹ and of diethyl ethylmalonate with ethyl tiglate.⁶⁰ Though no direct proof was obtained, this work tended to support the Holden-Lapworth view.^{59,61}

* An effort by Michael and Rosa⁶² to invalidate this conclusion, on the basis that the observed retrogression products could be derived from an adduct of two molecules of benzylideneacetophenone and one molecule of diethyl methylmalonate (see p. 308), foundered on their inability to prepare such a product from diethyl methylmalonate, in spite of its ready preparation from diethyl malonate.

⁵⁶ Michael and Rosa, *J. Am. Chem. Soc.*, **55**, 1632 (1933).

⁵⁷ Duff and Ingold, *J. Chem. Soc.*, 1934, 87.

⁵⁸ Rydon, *J. Chem. Soc.*, 1935, 420.

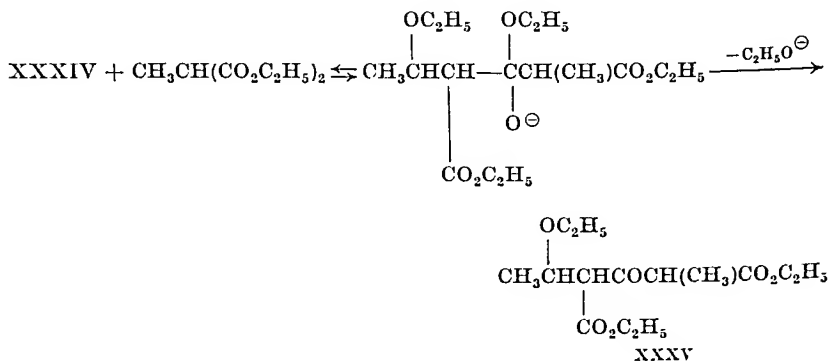
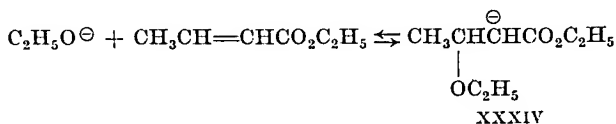
⁵⁹ Gardner and Rydon, *J. Chem. Soc.*, 1938, 45.

⁶⁰ Gardner and Rydon, *J. Chem. Soc.*, 1938, 48.

⁶¹ Gardner and Rydon, *J. Chem. Soc.*, 1938, 42.

⁶² Cf. Ingold and Rydon, *J. Chem. Soc.*, 1935, 857.

Attention has recently been called⁶² to the fact that higher yields of "abnormal" Michael products are often obtained from the usual starting materials than by subjecting the "normal" product (synthesized independently) to Michael reaction conditions. This appears to mean that the "normal" product is not necessarily an intermediate in the "abnormal" reaction. Consideration of the experimental results obtained in the condensation of ethyl crotonate and diethyl methylmalonate led to the following suggested pathway of reaction:⁶³ The full equivalent of base required for the abnormal reaction permits the assumption of initial bond formation between the reactants by a kind of Claisen condensation involving an anion (XXXIV) formed from the base and the acceptor.



Base-catalyzed loss of ethanol from intermediate XXXV would give the ester XXXVI. This ester may undergo an intramolecular Michael reaction with formation of the cyclobutanone intermediate XXXI postulated by Holden and Lapworth. Alternatively, it was suggested⁶³ that the cyclic intermediate may not have significant independent existence, but that the ester XXXVI can change directly to the observed abnormal product XXXVII by concerted alcoholysis and addition (see equations on p. 197).

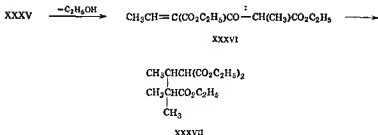
A recent kinetic study⁶⁴ of the abnormal reaction between diethyl fumarate and diethyl ethylmalonate showed that the donor anion and diethyl fumarate combine rapidly to form the anion of the normal product

⁶² P. R. Shafer, Ph. D. Thesis, University of Wisconsin, 1951.

⁶³ Shafer, Loeb, and Johnson, *J. Am. Chem. Soc.*, **75**, 5963 (1953).

⁶⁴ Tsuruta, Yasuhara, and Furukawa, *J. Org. Chem.*, **18**, 1246 (1953).

(distinguished from the abnormal product by specific gravity measurements) Isomerization of this anion to that of the abnormal product was observed to follow as a slow step. It was also observed that excess free diethyl ethylmalonate suppressed the abnormal reaction even when sodium ethoxide equivalent to the diethyl fumarate was present. This led to the deduction that the first-formed anion can be stabilized by the abstraction of hydrogen ion from free diethyl ethylmalonate in a fast reaction competitive with the isomerization



Definitive evidence that the "abnormal" reaction involves migration of a carboxyl group (in some form or other) has at last been obtained by isotopic tracer experiments. When ethyl crotonate containing C^{14} in the carbethoxyl group was condensed with diethyl methylmalonate, the product was found to result from migration of the labeled carbon atom.⁶⁰ Enrichment of carbethoxyl groups with O^{18} in ethyl crotonate, ethyl cinnamate, and diethyl methylmalonate provided further evidence that the condensation of either of the first two with the last (using one equivalent of base as catalyst to favor "abnormal" reaction) proceeds by carbethoxyl migration.⁶⁰⁻⁶²

With this evidence in hand, it can be firmly concluded that the Holden-Lapworth mechanism is basically correct, though the modifications suggested by Johnson⁶³ provide the most plausible view of the detailed reaction course.

The Question of Para-Bridged Intermediates

The condensation of 3-methyl-2-cyclohexenone (XXXVIII) and diethyl malonate presents features that have been rationalized^{64,70} in a fashion

⁶⁰ Shimamura, Inamoto, and Suhiro, *Bull. Chem. Soc. Japan*, **27**, 221 (1954) [*C.A.*, **49**, 7494 (1955)].

⁶¹ Swan, *J. Chem. Soc.*, 1955, 1039.

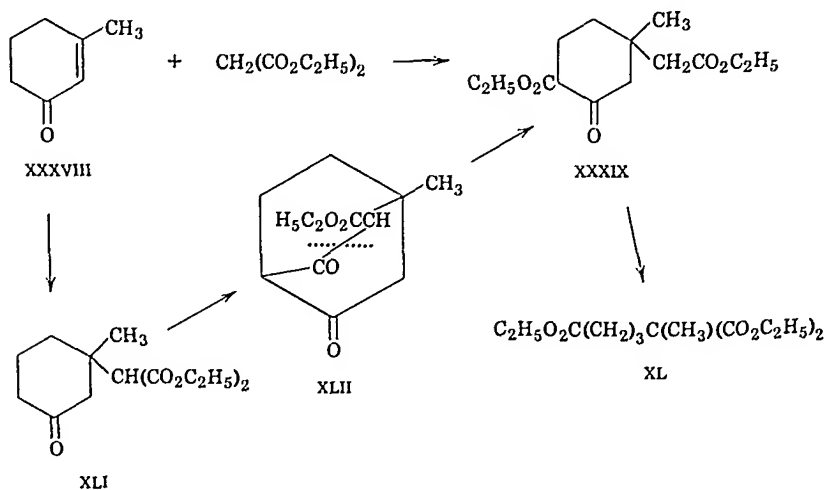
⁶² Samuel and Ginsburg, *J. Chem. Soc.*, 1955, 1298.

⁶³ Cf. Baker and Rothstein, *Chemistry & Industry*, 1955, 776.

⁶⁴ Farmer and Hows, *J. Chem. Soc.*, 127, 2358 (1925).

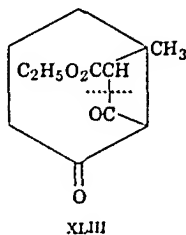
⁷⁰ Farmer and Hows, *J. Chem. Soc.*, 1926, 3223.

consistent with and tending to support the Holden-Lapworth cyclobutanone intermediate. Carried out at room temperature and with one equivalent of sodium ethoxide, the reaction leads to only one identified product, the diethyl ester XXXIX. At the temperature of boiling ethanol, this compound is accompanied by a product of ethanolysis, the open-chain triethyl ester XL.

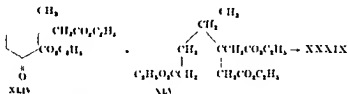


In this condensation, the "abnormal" position in which the carbethoxy portion of the donor molecule appears is para rather than ortho on the alicyclic ring. By way of explanation, it has been postulated that the primary product would be XLI, from the normal condensation; this was believed to be converted by a Dieckmann reaction into the bicyclic diketone XLII. Ethanolysis of the diketone in the manner indicated by the broken line was believed to lead to XXXIX.

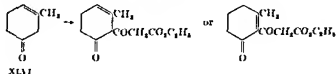
This mechanism was advanced as a parallel to the Holden-Lapworth formulation, but with a cyclohexanone rather than a cyclobutanone intermediate because formation of a para bridge where possible (as in this instance) is more favorable than the alternative XLIII.



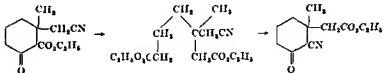
However, the suggestion has recently been made⁴² that a para-bridged intermediate may not be formed in such instances. Instead the expected product of the abnormal Michael reaction, XLIV, may be first produced, and this may undergo ethanolysis (reverse Dieckmann) to give the open-chain triester XLV, which then cyclizes (in a known reaction) to XXXIX.



In any case, it has been shown that the normal adduct XLI is not the precursor of XXXIX, since the latter is produced in higher yield from 3-methyl-2-cyclohexenone and diethyl malonate than from XLI.⁴³ It is suggested,⁴² as in the case mentioned above, that the first step is an ester condensation, either at position 6 (which would involve subsequent para bridging) or more probably at position 2 via the anion XLVI



This explanation is based on a parallel with the mechanism for the reaction of 3-methyl-2-cyclohexenone with ethyl cyanoacetate, which was outlined on the basis of detailed evidence as involving the following succession of intermediates:



Stereochemistry of the Michael Condensation

Little is known about the stereo course of the Michael condensation, although the formation of asymmetric carbon atoms in open-chain products and the possibility of *cis-trans* isomerism in alicyclic adducts

raise a number of stereochemical problems. The formation of diastereomeric adducts has often been noted, e.g., with the following reactants: benzylideneacetone and dimethyl malonate;⁷¹ benzylideneacetophenone and benzyl cyanide;⁷² diethyl succinate,⁷³ and *p*-tolyl benzyl sulfone;⁷⁴ α -benzylidenepropiophenone and dimethyl malonate;^{75,76} ethyl cinnamate and diethyl methylmalonate;^{50,77} ethyl β -isopropylacrylate and ethyl cyanoacetate;⁷⁸ ethyl cinnamate and ethyl cyanoacetate;^{79,80} ethyl phenylacetate,^{81,82} or benzyl cyanide;^{27,83,84} cinnamionitrile and *m*-aminobenzyl cyanide;²⁷ 2-nitro-2-butene and benzyl cyanide,⁸⁵ 2-nitro-1-phenyl-1-propene and diethyl malonate;⁸⁶ α -nitrostilbene and diethyl malonate;⁸⁶ and 3-cyano-1,2,5,6-tetrahydropyridine and diethyl malonate.⁸⁷

In the condensation of ethylideneacetone with 7-chloro-4,6-dimethoxycoumaran-3-one, two possible isomers are formed simultaneously;⁸⁸ a similar result was obtained in the condensation with the chlorine-free analog. The reaction between 4-methylcyclohexanone and methyl isopropenyl ketone also leads to two stereoisomeric forms of 3,6-dimethyl-9-hydroxy-2-decalone.⁸⁹

The reaction pairs benzylideneacetophenone-benzyl cyanide⁷² and α -benzylidenepropiophenone-dimethyl malonate^{75,76} represent two different ways in which asymmetric carbon atoms can be formed as a result of a Michael condensation. In the adduct XLVII the α - and β -carbon atoms of the acceptor become asymmetric; in the adduct XLVIII the β -carbon atom of the acceptor and the carbon atom of the donor molecule that is linked to the acceptor become the centers of asymmetry. In view of the undoubted ability of the alkaline condensing agent to invert configuration around carbon atoms substituted as in $-\text{CH}(\text{CH}_3)\text{COC}_6\text{H}_5$

⁷¹ Qudrat-I-Khuda, *J. Indian Chem. Soc.*, **8**, 215 (1931) [*C.A.*, **26**, 123 (1932)].

⁷² Kohler and Allen, *J. Am. Chem. Soc.*, **46**, 1522 (1924).

⁷³ Stobbe, *Ann.*, **314**, 111 (1901).

⁷⁴ Connor, Fleming, and Clayton, *J. Am. Chem. Soc.*, **58**, 1386 (1936).

⁷⁵ Kohler, *Am. Chem. J.*, **46**, 474 (1911).

⁷⁶ Kohler and Davis, *J. Am. Chem. Soc.*, **41**, 992 (1919).

⁷⁷ Michael and Ross, *J. Am. Chem. Soc.*, **53**, 1150 (1931).

⁷⁸ Howles, Thorpe, and Udall, *J. Chem. Soc.*, **77**, 942 (1900).

⁷⁹ Carter and Lawrence, *Proc. Chem. Soc.*, **18**, 178 (1900).

⁸⁰ Avery and McGrew, *J. Am. Chem. Soc.*, **57**, 208 (1935).

⁸¹ Badger, Campbell, and Cook, *J. Chem. Soc.*, **1949**, 1084.

⁸² Borsche, *Ber.*, **42**, 4496 (1909).

⁸³ Avery, *J. Am. Chem. Soc.*, **50**, 2512 (1928).

⁸⁴ Avery and McDole, *J. Am. Chem. Soc.*, **30**, 1423 (1908).

⁸⁵ Buckley, Hunt, and Lowe, *J. Chem. Soc.*, **1947**, 1504.

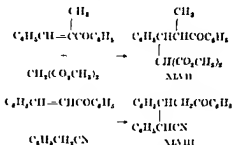
⁸⁶ Boberg and Schultze, *Chem. Ber.*, **88**, 74 (1955).

⁸⁷ Wohl and Losanitsch, *Ber.*, **40**, 4638 (1907).

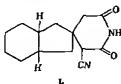
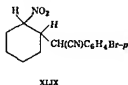
⁸⁸ MacMillan, Mulholland, Dawkins, and Ward, *J. Chem. Soc.*, **1954**, 429.

⁸⁹ Colonge, Dreux, and Kehlstaedt, *Compt. rend.*, **238**, 693 (1954).

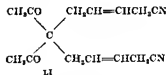
and $-\text{CH}(\text{CN})\text{C}_6\text{H}_5$, the product isolated must be an equilibrium mixture of all possible forms. The isolation of diastereomerides from product mixtures is then evidence that the forms involved are approximately equal energetically.



Both *cis* and *trans* forms arise in the condensation of 1-nitrocyclohexene with *p*-bromobenzyl cyanide to XLIX,⁹⁵ whereas only one isomer (L) is formed from *cis*-2-hydrindylideneacetone nitrile and cyanoacetamide.⁹⁶



One unsaturated Michael adduct LI appears in *cis* and *trans* isomeric forms; this is the product of the reaction between acetylacetone and 2 moles of 1-cyanobutadiene.⁹¹



When only one adduct is formed, the determination of its configuration is usually difficult due to the lack of reference compounds of established configuration. However, it has been proved that the dicyclic compounds formed from acyl- or carboxy-cyclohexenes frequently, if not generally, have the *trans* configuration. This applies to the following cases: ethyl cyclopentenecarboxylate with ethyl cyanoacetate or diethyl malonate

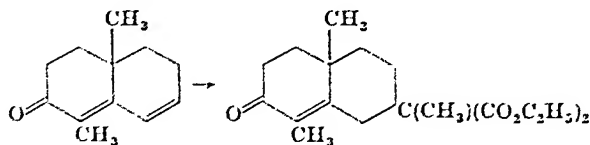
⁹⁵ Kandiah, *J. Chem. Soc.*, 1931, 922.

⁹⁶ Charlsh, Davies, and Rose, *J. Chem. Soc.*, 1948, 232.

(*trans* only);⁹² acetylcyclohexene and ethyl acetoacetate (*trans* only);⁹³ acetylcyclohexene and diethyl malonate (*cis* and *trans*);⁹⁴⁻⁹⁶ 2-methyl-1-butyrylcyclohexene and diethyl malonate (*trans* only);⁹⁶ 2,6-dimethyl-butyrylcyclohexene and diethyl malonate (*trans* only);⁹⁶ vinyl cyclohexenyl ketone and diethyl malonate (*trans* only);¹⁰⁰ 4-methoxy- and 3,4-methylenedioxy-benzalacetophenone and 3-methylcyclohexanone (*cis* and *trans*);^{100a} methyl isopropenyl ketone and 3- and 4-methylcyclohexanone (*cis* and *trans*);¹⁰¹ and (+)-dihydrocarvone and 1-diethylamino-3-pentanone methiodide (*cis* and *trans*).¹⁰²

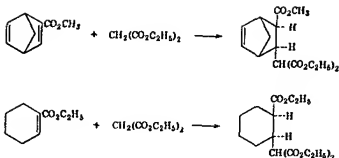
Isomers have also been formed in the self-condensation of 1-acetyl-1-cyclohexene^{97,98} and in the condensation of 1-acetyl-1-cyclohexene with 1-tetralone.⁹⁹

In the total synthesis of santonin,¹⁰³ use was made of the fact that the Michael condensation of diethyl methylmalonate and 1,10-dimethyl-2-oxo-2,3,4,5,6,10-hexahydronaphthalene introduces the side chain so that

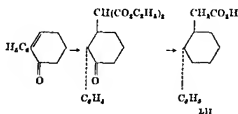


it is *cis* to the methyl group at C₁₀.¹⁰⁴ An analogous observation has been made for 3,5-cholestadien-7-one.

Cis addition is observed in the addition of diethyl malonate, diethyl methylmalonate, and ethyl acetoacetate to methyl bicyclo[2.2.1]hepta-2,5-diene-2-carboxylate^{104a} and in the addition of diethyl malonate to ethyl 1-cyclohexene-1-carboxylate.^{104b}



A tendency for *trans* addition is evident in the Michael condensation of 2-aryl-2-cyclohexen-1-ones. Here it has been shown with diethyl malonate that a *trans* compound is obtained, for the product could be related to the known *trans*-2-phenylcyclohexylacetic acid (LII)^{105,106}



It has further been demonstrated that the addition of dibenzyl malonate to 4-phenyl- or 5-phenyl-2-cyclohexenone¹⁰⁷ and of methyl nitroacetate to 2-phenyl-2-cyclohexenone takes the same steric course.¹⁰⁸

SCOPE AND LIMITATIONS

Donors

All of the donor molecules appearing in Tables I-XXI are collected in Table XXII. In the almost complete absence of kinetic studies of the Michael condensation, an exact comparison of the compounds acting as donors in the condensation is impossible. However, in some cases in which the donor contains two active hydrogen atoms, the efficacy of the

¹⁰⁵ Bachmann and Fornfeldt, *J. Am. Chem. Soc.*, 72, 5529 (1950)

¹⁰⁶ Ginsburg and Pappo, *J. Chem. Soc.*, 1951, 938.

¹⁰⁷ Bergmann and Szmarzanski, *J. Am. Chem. Soc.*, 75, 3226 (1953)

¹⁰⁸ Ginsburg and Pappo, *J. Chem. Soc.*, 1953, 1524

activating groups can be compared directly. For example, two carbethoxy groups activate hydrogen more than one carbethoxy¹⁰⁹ or one aldehyde group,¹¹⁰ but one carbonyl group is more effective than one carbethoxy group.¹¹¹ The groups $\text{CH}(\text{CH}_3)$ and $\text{CH}(\text{C}_6\text{H}_5)$ have greater activating power than a methylene group,¹¹²⁻¹¹⁵ and a nitro group is a more powerful activator than a carbethoxy¹¹⁶ or an alkylsulfonyl group.¹¹⁷ It also appears to be generally true that unsaturated ketones are more reactive than nitriles and nitriles more than esters, and that α,β -unsaturated sulfones are least reactive.¹¹⁸⁻¹²² The behavior of methyl β -cyanoethyl ketone in Michael additions¹²³ confirmed the stronger activating influence of a carbonyl group as opposed to a nitrile group. Recent work¹²⁴ has shown that the phosphonate group $-\text{PO}(\text{OR})_2$ also activates hydrogen atoms on the adjoining carbon atom. Like the nitro and sulfoxide functions, it also activates neighboring double bonds to act as acceptors (see Table XXI).

Though one would expect the reactivity of a donor to be related to the degree of enolization in the reaction environment, no simple relationship was found between reactivity and the tendency of the donor to enolize in the pure state.¹²⁵ Likewise, the reactivity of a methylene or methine group toward a Grignard reagent (Zerewitinoff test) does not appear to parallel its activity as a donor in the Michael reaction.¹²⁶

Generally speaking, one would expect that the degree to which the Michael reaction takes place, as well as its rate, should be importantly influenced by the acidity of the donor and the polarity of the carbon-carbon double bond in the acceptor. As to the former, the acidity of the hydrogen atom in the group RCH decreases in the following sequence:

¹⁰⁹ Friedmann, *J. prakt. Chem.*, [2], **146**, 79 (1936).

¹¹⁰ Moe, Warner, and Buckley, *J. Am. Chem. Soc.*, **73**, 1002 (1951).

¹¹¹ Hill, *Am. Chem. J.*, **24**, 1 (1900).

¹¹² Bachmann and Wick, *J. Am. Chem. Soc.*, **72**, 3388 (1950).

¹¹³ Boekelheide, *J. Am. Chem. Soc.*, **69**, 790 (1947).

¹¹⁴ Frank and Pierle, *J. Am. Chem. Soc.*, **73**, 724 (1951).

¹¹⁵ Wilds, Ralls, Wildman, and McCaleb, *J. Am. Chem. Soc.*, **72**, 5704 (1950).

¹¹⁶ Leonard, Felloy, and Nicolaides, *J. Am. Chem. Soc.*, **74**, 1700 (1952).

¹¹⁷ Buckley, Elliott, Hunt, and Lowe, *J. Chem. Soc.*, **1947**, 1505.

¹¹⁸ Truce and Wellisch, *J. Am. Chem. Soc.*, **74**, 2881 (1952).

¹¹⁹ Henecka, *Chem. Ber.*, **81**, 197 (1948).

¹²⁰ Henecka, *Chem. Ber.*, **82**, 41 (1949).

¹²¹ Henecka, *Chem. Ber.*, **82**, 104 (1949).

¹²² Henecka, *Chem. Ber.*, **82**, 112 (1949).

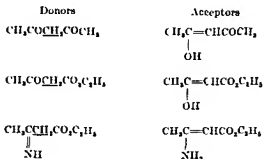
¹²³ Chem. Werke Huels, Ger. pat. 811,231 [*C.A.*, **47**, 11234 (1953)].

¹²⁴ Pudovik and Lebedeva, *Zhur. Obshchei Khim.*, **22**, 2128 (1952) [*C.A.*, **48**, 564 (1954)].

¹²⁵ Connor and Andrews, *J. Am. Chem. Soc.*, **56**, 2713 (1934).

¹²⁶ McAlpine and Ongley, *Anal. Chem.*, **27**, 55 (1955).

$R = \text{NO}_2 > \text{SO}_2\text{R} > \text{CN} > \text{CO}_2\text{R} > \text{CHO} > \text{COR}$.¹²⁷ As to the latter, the electromeric effects of the activating groups which produce polarity in the double bond diminish in the sequence $\text{CHO} > \text{COR} > \text{CN} > \text{CO}_2\text{R} > \text{NO}_2$. Through possession of appropriate combinations of these groups, certain substances, e.g., β -diketones, β -keto esters or ethyl β -aminocrotonate, can act either as donors or acceptors



Reactions with Cyclopropane Derivatives

A few cyclopropane derivatives have been observed to participate in the Michael condensation. In the reaction of ethyl 1-cyanocyclopropane-1-carboxylate (LIII) with both ethyl cyanoacetate¹²⁹ and diethyl malonate,¹²⁹ ring scission occurs.¹²⁹⁻¹³³ The intermediates LIV and LV cyclize to the corresponding cyclopentanoneimide derivatives LVI and LVII, subsequent elimination of the cyano and the second carboxy group, respectively, leads to diethyl cyclopentanone-2,5-dicarboxylate (LVIII). In the analogous reaction between diethyl malonate and diethyl cyclopropane-1,1-dicarboxylate, the same cyclopentanone derivative, LVIII, formed via tetraethyl butane-1,1,4,4-tetracarboxylate can be isolated.^{130,134} The similarity between a double bond and the cyclopropane ring illustrated by this reaction is supported by other

¹²⁷ Arndt, Scholz, and Frobel, *Ann.*, 521, 111 (1936)

¹²⁸ Thorpe, *J. Chem. Soc.*, 95, 1901 (1909)

¹²⁹ Mitchell and Thorpe, *J. Chem. Soc.*, 97, 997 (1910)

¹³⁰ Bone and Perkin, Jr., *J. Chem. Soc.*, 67, 108 (1895)

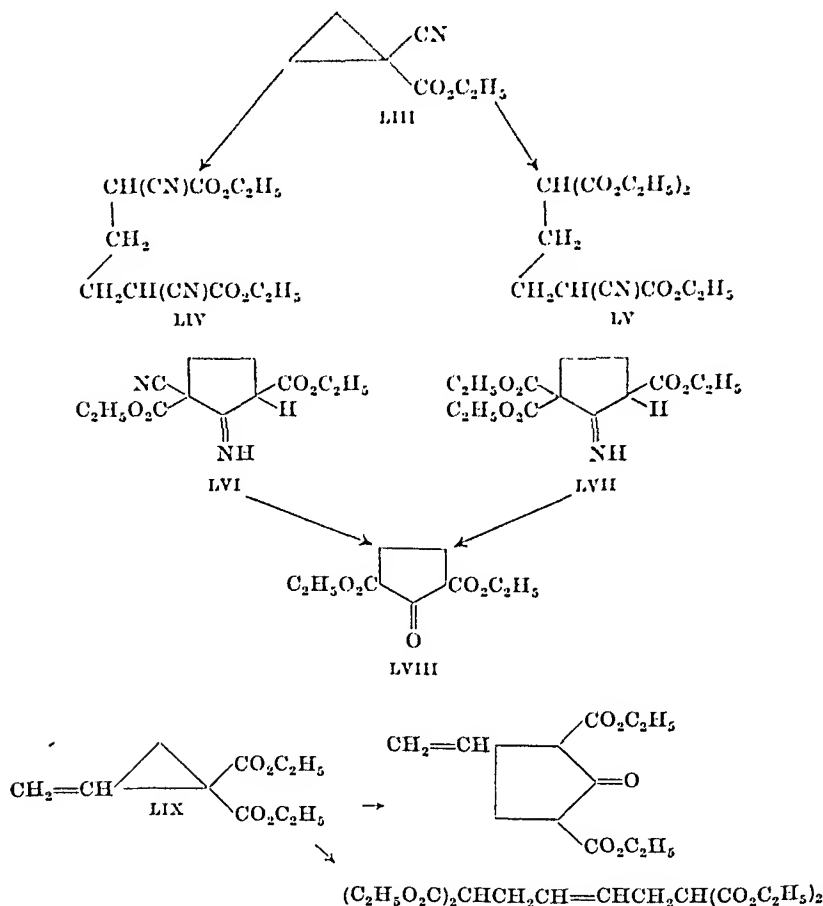
¹³¹ Cf. Fittig and Roeder, *Ann.*, 227, 13 (1885)

¹³² Cf. Best and Thorpe, *J. Chem. Soc.*, 95, 697, 699 (1909).

¹³³ Radulescu, *Ber.*, 44, 1018 (1911)

¹³⁴ Kierstead, Lunstead, and Weedon, *J. Chem. Soc.*, 1952, 3616.

evidence,¹³⁵⁻¹⁴⁴ particularly by the recent experiments showing that the enolate of diethyl malonate undergoes a Michael reaction with diethyl 2-vinylcyclopropane-1,1-dicarboxylate (LIX);¹³⁴ this partly follows the



¹³⁵ Cf. Klotz, *J. Am. Chem. Soc.*, **66**, 88 (1944); Roberts and Green, *ibid.*, **68**, 214 (1946); Rogers, *ibid.*, **69**, 2544 (1947); cf. ref. 137.

¹³⁶ Kierstead, Linstead, and Weedon, *J. Chem. Soc.*, 1952, 3610.

¹³⁷ Mariella, Peterson, and Ferris, *J. Am. Chem. Soc.*, **70**, 1494 (1948).

¹³⁸ Smith and Rogier, *J. Am. Chem. Soc.*, **73**, 3831 (1951).

¹³⁹ Smith and Rogier, *J. Am. Chem. Soc.*, **73**, 3840 (1951).

¹⁴⁰ Mariella and Raube, *J. Org. Chem.*, **18**, 282 (1953).

¹⁴¹ Greenfield, Friedel, and Orchin, *J. Am. Chem. Soc.*, **76**, 1258 (1954).

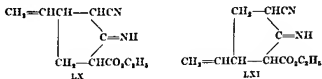
¹⁴² Perold, *J. S. African Chem. Inst.*, **6**, 22 (1953) [*C.A.*, **48**, 4314 (1954)].

¹⁴³ Eastman, *J. Am. Chem. Soc.*, **76**, 4115 (1954).

¹⁴⁴ Eastman and Selover, *J. Am. Chem. Soc.*, **76**, 4118 (1954).

above scheme, but partly takes place at the ends of the "conjugated" system. Both reactions occur also in $\alpha,\beta,\gamma,\delta$ doubly unsaturated carboxylic acid derivatives (see p 237).

A similar study has been made¹⁴⁵ of the reaction of ethyl cyanoacetate with ethyl 1-cyano-2-vinylcyclopropane-1-carboxylate, synthesized *in situ* from *trans*-1,4-dibromo-2-butene and ethyl cyanoacetate. The product, obtained in 30% yield, was a mixture of the two cyclopentane derivatives LX and LXI



The System $\text{C}=\text{C}-\text{C}=\text{N}$

The system $\text{C}=\text{C}-\text{C}=\text{N}$ behaves like the system $\text{C}=\text{C}-\text{C}=\text{O}$ in the Michael reaction. The most extensive studies, on the addition of reactive methylene compounds to quinone imides, have been summarized^{145a} selected examples are given in Table IX.

2-Vinylpyridine and 4-vinylpyridine are suitable acceptors for the Michael reaction (Table XXI). Analogously, phenanthridine-9-carboxaldehyde reacts with 9-methylphenanthridine (LXII) to give 1,2,3-tri-(9-phenanthridyl)propane (LXIII),¹⁴⁶ undoubtedly as shown on page 208. The formation of diethyl 4-methyl-5-acetylpyridine-2,6-dicarboxylate (LXVIII) from ethyl acetylpyruvate (LXIV) and ammonia¹⁴⁷ appears to result from reaction of part of the ester with ammonia to give the imine of its enolic form and a subsequent Michael condensation between the latter and the keto form of the original ester or its imine.

In this connection, it should be mentioned that Schiff bases of the benzylideneaniline type (but not ketone anils) add, for example, ethyl acetoacetate,¹⁴⁸⁻¹⁵⁰ ethyl oxaloacetate,^{148,151} diethyl malonate,¹⁵² ethyl

¹⁴⁵ Kierstead, Lunstead, and Weedon, *J. Chem. Soc.*, 1953, 1799.

^{145a} Adams and Reifschneider, *Bull. soc. chim. France*, 1958, 23.

¹⁴⁶ Caldwell, *J. Chem. Soc.*, 1952, 2035.

¹⁴⁷ Mumm and Bergell, *Ber.*, 45, 3040 (1912).

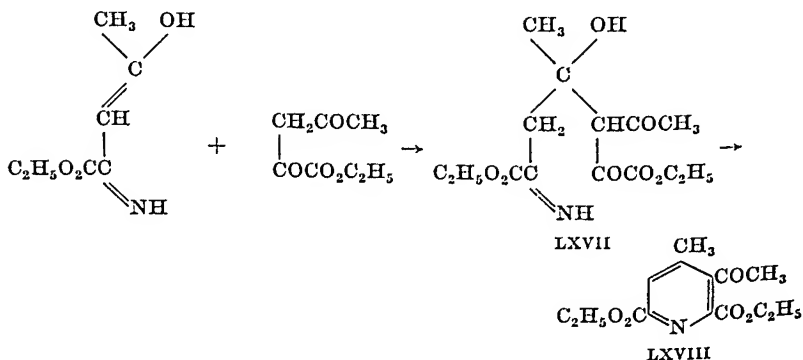
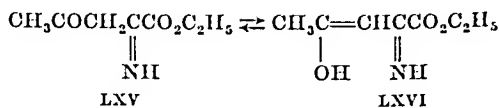
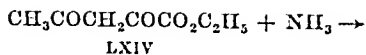
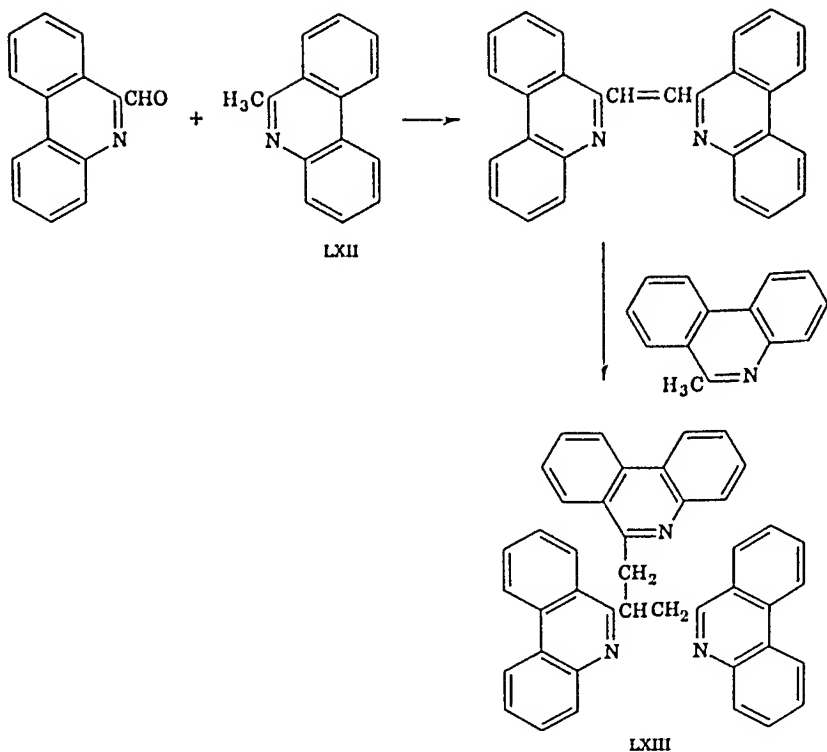
¹⁴⁸ Schiff and Bertoni, *Ber.*, 30, 601 (1897).

¹⁴⁹ Schiff, *Ber.*, 31, 205 (1898).

¹⁵⁰ Schiff, *Ber.*, 31, 601 (1898).

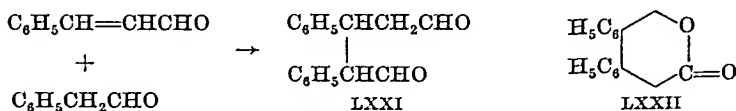
¹⁵¹ Philpott and Jones, *J. Chem. Soc.*, 1933, 337.

¹⁵² Betti, *Gazz. chim. Ital.*, 30, II, 301 (1900).



cyclohexanone-2-carboxylate) leads to derivatives of δ -aldehyde acids. Alkyl substitution in the α position does not appear to influence adversely the ability of the aldehydes to undergo Michael condensation; β substitution, on the other hand, alters the course of the reaction.^{157,158} (For further synthetic uses of the condensation products see p. 249.)

There are very few examples of condensations between α,β -ethylenic aldehydes and ketones or aldehydes. In the aldehyde- α,β -ethylenic aldehyde condensations secondary reactions regularly accompany the condensation.¹⁶³⁻¹⁶⁵ For example, the product to be expected from the interaction between cinnamaldehyde and phenylacetaldehyde, the dialdehyde LXXI, undergoes an intramolecular Cannizzaro reaction to yield δ -hydroxy- β,γ -diphenylvaleric acid, isolated as its lactone LXXII.



The "dimerization" of α,β -unsaturated aldehydes such as 2-ethyl-2-hexenal which takes place under the influence of aqueous-alcoholic alkali has been explained as a Michael reaction followed by intramolecular aldolization to yield a cyclic product.^{165a}

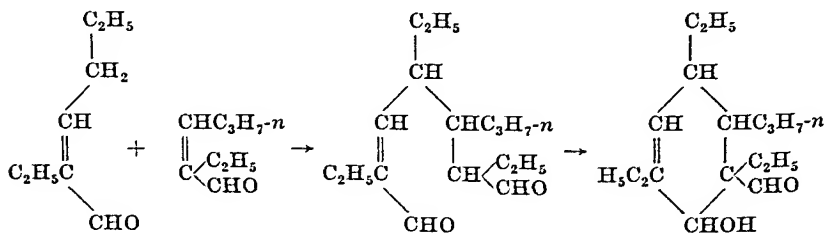


Table I includes some acceptors having a hydroxy (or alkoxy or amino) group attached to the double bond, i.e., they are the enolic forms of compounds that can also function as donors in the Michael reaction (see p. 205). All primary condensation products from donors that contain a $\text{C}=\text{NH}$ group in the immediate vicinity of the reactive methylene group spontaneously cyclize with elimination of the hydroxy (alkoxy, amino) groups to yield pyridine derivatives.¹⁶⁶

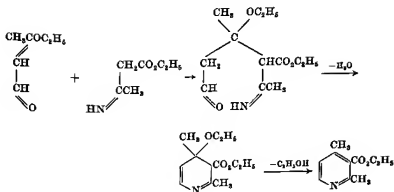
¹⁵⁵ Meerwein, *J. prakt. Chem.*, [2], 97, 225 (1918).

¹⁵⁶ Hucusermann, *Helv. Chim. Acta*, 34, 1462 (1951).

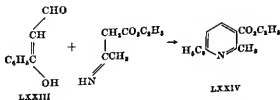
¹⁵⁷ Meerwein, *Ber.*, 53, 1829 (1920).

¹⁵⁸ Nielsen, *J. Am. Chem. Soc.*, 79, 2518, 2524 (1957).

¹⁵⁹ Dornow, *Ber.*, 72, 1543 (1939). Compare, Baumgarten and Dornow, *Ber.*, 72, 563 (1939).



However, the course of cyclization can sometimes vary. From benzoylacetaldehyde and ethyl β -aminocrotonate one does not obtain the expected ethyl 2-methyl-4-phenylpyridine-3-carboxylate, but the 6-phenyl isomer LXXIV.¹⁶⁷ This probably results from the reaction of benzoyl-acetaldehyde as β -hydroxycinnamic aldehyde (LXXIII) or as hydroxy-methyleneacetophenone.



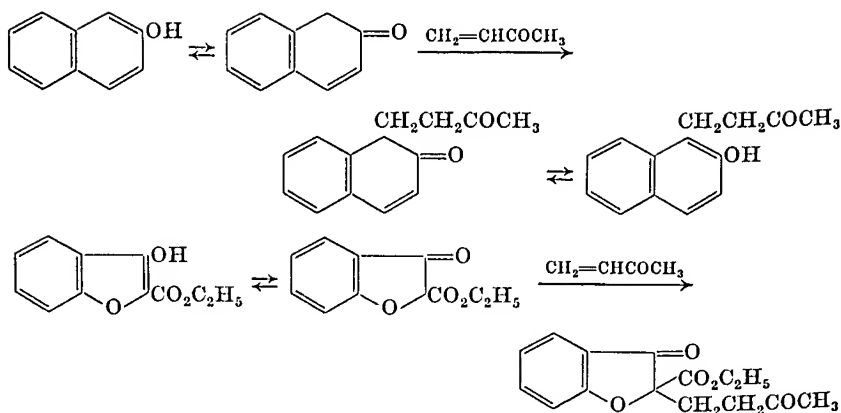
Aliphatic α,β -Ethylenic Ketones (Table II). The Michael condensation of aliphatic α,β -ethylenic ketones proceeds normally; the yields reported are often very high. The ease with which the ethylenic ketones undergo the condensation is exemplified by the fact that substances such as β -naphthol¹⁶⁸ or ethyl 3-hydroxy-4,5-benzofuran-2-carboxylate¹⁶⁹ react with methyl vinyl ketone in their ketonic forms. The same is true for the reactions of 4-hydroxycoumarin with ethylideneacetone and mesityl oxide, respectively.¹⁶⁹ Compare also the reaction of kojic acid with acrylonitrile.¹⁷⁰

¹⁶⁷ Spaeth and Burger, *Monatsh.*, **49**, 265 (1918).

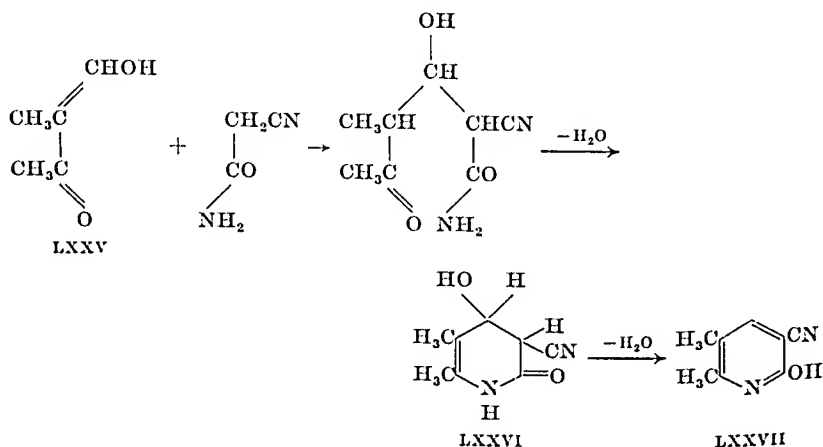
¹⁶⁸ Miller and Robinson, *J. Chem. Soc.*, 1934, 1535

¹⁶⁹ Ikawa, Stahmann, and Lusk, *J. Am. Chem. Soc.*, **66**, 902 (1944)

¹⁷⁰ Woods, *J. Am. Chem. Soc.*, **74**, 3959 (1952)



An example of the reaction of hydroxymethylene ketones is seen in the condensation of the methyl ethyl ketone derivative LXXV with cyanoacetamide (under the catalytic influence of pyridine or piperidine).^{171,172} The primary product cyclizes spontaneously and, dependent on the operating conditions, 2-keto-3-cyano-4-hydroxy-5,6-dimethyl-1,2,3,4-tetrahydropyridine (LXXVI) or its dehydration product, 2-hydroxy-3-cyano-5,6-dimethylpyridine (LXXVII), is obtained.

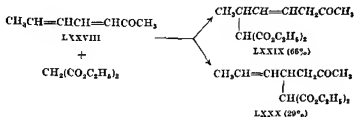


Mention should finally be made of the behavior of doubly unsaturated ketones. Of this group, two types have been somewhat cursorily investigated. Crotylideneacetone (LXXVIII) yields with diethyl malonate

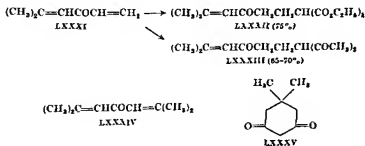
¹⁷¹ Tracy and Elderfield, *J. Org. Chem.*, **6**, 63 (1941).

¹⁷² Joshi, Kaushal, and Deshapande, *J. Indian Chem. Soc.*, **18**, 479 (1941) [*C.A.*, **36**, 4182 (1942)].

in the presence of sodium methoxide a mixture of two substances, of which the predominant one, LXXIX, results from 1,6 addition, the isomer LXXX from 1,4 addition.¹⁷³ 5-Methyl-1,4-hexadien-3-one (LXXXI) reacts, under the influence of sodium methoxide, both with diethyl



malonate and acetylacetone at the less-substituted end of the molecule only, giving LXXXII and LXXXIII, respectively.¹⁷⁴ Phorone (LXXXIV) does not react analogously to LXXXI with diethyl malonate in alcoholic solution. Instead the product obtained, LXXXV,¹⁷⁵ is identical with that obtained from mesityl oxide.¹⁷⁶⁻¹⁷⁹ Apparently



phorone reverts to mesityl oxide more quickly than it reacts with the malonate, or the adduct formed suffers retrogression.

α,β -Acetylenic Ketones. Acetylenic ketones that contain the triple bond in the $\alpha\beta$ position would be expected to give α,β -olefinic ketones in

¹⁷³ Farmer and Mehta, *J. Chem. Soc.*, 1931, 1904.

¹⁷⁴ Nazarov and Terekhova, *Bull. Acad. Sci. U.R.S.S. Class. Sci. Chem.*, 1946, 201 [C.A., 42, 7729 (1948)].

¹⁷⁵ Vorlaender and Gaertner, *Ann.*, 204, 1 (1899).

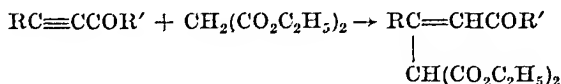
¹⁷⁶ Komppa, *Ber.*, 32, 1421 (1899).

¹⁷⁷ Scherer and Todd, *Org. Syntheses Coll. Vol. 2*, 200 (1950).

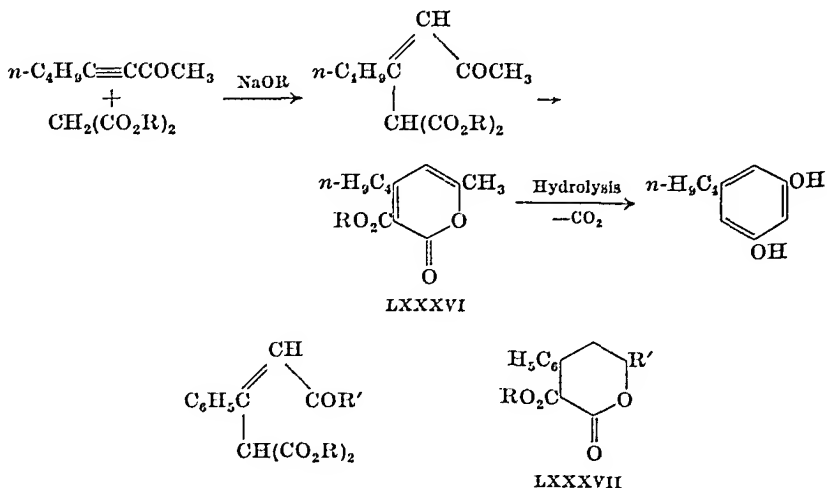
¹⁷⁸ Vorlaender, *Ann.*, 294, 273 (1897).

¹⁷⁹ Vorlaender and Ling, *Ann.*, 294, 302 (1897).

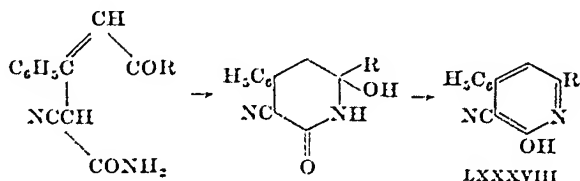
the Michael condensation, as shown in the formulation. In the cases investigated (acetyl-*n*-butylacetylene,¹⁸⁰ propionylphenylacetylene,¹⁸¹



benzoylphenylacetylene,¹⁸² benzoyl-*o*-chlorophenylacetylene¹⁸³), the primary products from malonic esters and the corresponding sodium alkoxides as catalysts proved too reactive to be isolated; cyclization products were isolated instead. From acetyl-*n*-butylacetylene, the α -pyrone derivative LXXXVI, which could be converted to 5-*n*-butyl-resorcinol, was obtained. The phenylacetylene derivatives also cyclized



to yield α -pyrones, LXXXVII.^{181,182} Analogously, the reaction between cyanoacetamide and propionylphenylacetylene¹⁸¹ or benzoylphenylacetylene¹⁸⁴ leads to the substituted 2-pyridols, LXXXVIII. From



¹⁸⁰ Anker and Cook, *J. Chem. Soc.*, 1945, 311.

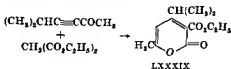
¹⁸¹ Barilhan, *J. Chem. Soc.*, 1929, 2223.

¹⁸² Kohler, *J. Am. Chem. Soc.*, 44, 379 (1922).

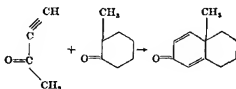
¹⁸³ Bickel, *J. Am. Chem. Soc.*, 72, 1022 (1950).

¹⁸⁴ Barat, *J. Indian Chem. Soc.*, 7, 851 (1930) [*C.A.*, 25, 2145 (1931)].

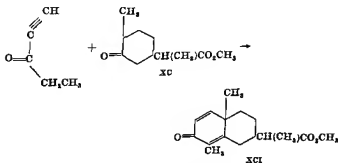
5-methyl-3-hexyn-2-one and diethyl malonate in the presence of a small quantity of sodium ethoxide 3-carbethoxy-4-isopropyl-6-methyl- α -pyrone (LXXXIX) was obtained in 59% yield.¹⁸⁵



Cyclization also takes place in the reaction between methyl ethynyl ketone and 2-methylcyclohexanone. Under the influence of sodium hydride, 2-keto-10-methyl-2,5,6,7,8,10-hexahydronaphthalene is formed.¹⁸⁶



In the Michael condensation between ethyl ethynyl ketone and the cyclohexanone derivative XC under the influence of sodium triphenylmethide, very low yields of XCI were obtained,¹⁸⁷ cf. refs. 188 and 189. As similar unsatisfactory results had been recorded in analogous



¹⁸⁴ Smith and Kelly, *J. Am. Chem. Soc.*, **74**, 3305 (1952).

¹⁸⁵ Woodward and Singh, *J. Am. Chem. Soc.*, **72**, 494 (1950).

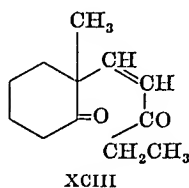
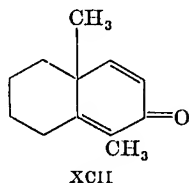
¹⁸⁶ Cleme and McQuillin, *J. Chem. Soc.*, 1952, 3839.

¹⁸⁷ Gunstone and Tulloch, *J. Appl. Chem. London*, **4**, 291 (1954).

¹⁸⁸ Abe, Harukawa, Ishikawa, Miki, Sumi, and Toge, *Proc. Japan. Acad.*, **28**, 425 (1952).

[*C. A.*, **48**, 1317 (1954)].

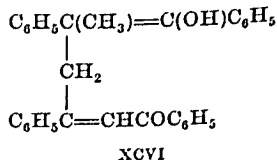
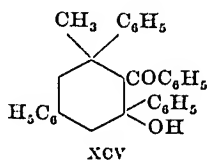
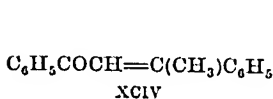
reactions,^{190,191} a systematic study of the reaction between 2-methylcyclohexanone (in the form of its metal enolates) and ethyl ethynyl ketone, formed in situ, was undertaken. However, β -chlorovinyl ethyl ketone, β -ethoxyvinyl ethyl ketone, and β -propionylvinylpyridinium chloride gave about the same yields as ethyl ethynyl ketone itself; and β -dimethylaminovinyl ethyl ketone did not react at all with the sodium enolate. Moreover, in addition to the expected 1,10-dimethyl-2-keto-2,5,6,7,8,10-hexahydronaphthalene (XCII), the open-chain product 2-methyl-2-(β -propionylvinyl)cyclohexanone (XCIII) was formed. A



considerable advantage was noted in use of the calcium or the lithium enolate of 2-methylcyclohexanone with β -chlorovinyl ethyl ketone; these gave yields of 12–14 and 20%, respectively, whereas the sodium enolate gave only 3–4%.

Aromatic α,β -Ethylenic Ketones (Tables III, IV). The introduction of aromatic radicals into the terminal positions of the system $C=C-C=O$ appears to increase its polar character and therefore its tendency to undergo the Michael condensation. Perhaps it is for this reason that a very large number of such reactions has been carried out. Those in which the ketone is unsaturated on only one side are summarized in Table III, in which the following order is observed: vinyl phenyl ketones, methyl styryl ketones, phenyl styryl ketones.

The unsaturated ketone dypnone (XCIV) undergoes self-condensation when treated with alkali. The product "dypnopinacol" has been given the formula XCV.¹⁹¹⁻¹⁹³ Although XCVI has been assumed to be an intermediate,^{191,192} it seems quite unlikely that the methyl group has a



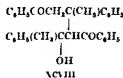
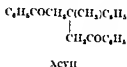
¹⁹⁰ Gunstone and Heggie, *J. Chem. Soc.*, 1952, 1437.

¹⁹¹ Iwanow and Iwanow, *Ber.*, 76, 988 (1943).

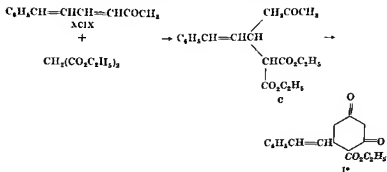
¹⁹² Iwanow and Iwanow, *Ber.*, 76, 1148 (1943).

¹⁹³ Meerwein, *Ber.*, 77, 229 (1944).

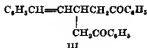
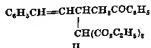
sufficiently reactive hydrogen to act as a donor. It is suggested by the authors that some of the dyprnone is hydrolyzed to acetophenone by analogy with the known hydrolysis of mesityl oxide. Acetophenone then gives the diketone XCVII by Michael condensation; the diketone condenses with another molecule of acetophenone to yield the aldol XCVIII, which cyclizes normally to dypnopinacol



Few doubly unsaturated ketones of the type $\text{C}_6\text{H}_5\text{CH}=\text{CHCH}=\text{CHCOR}$ appear to have been studied. When cinnamylideneacetone (XCIX) is treated with diethyl malonate and sodium ethoxide, 1,4 addition takes place. The primary product C cyclizes spontaneously, leading to



4-carbethoxy-5-styrylcyclohexane-1,3-dione (I).^{176,194,195} Cinnamylideneacetophenone also gives the 1,4 addition products II and III, respectively, with diethyl malonate and sodium ethoxide,¹⁹⁶ and with acetophenone



* Enumeration of formulas begins with I again after C to reduce the complexity of the numbers

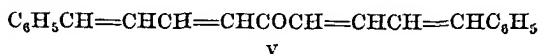
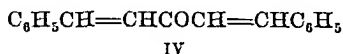
¹⁷⁶ Vorlaender, *Ber.*, 36, 2339 (1903).

¹⁹⁴ Vorlaender and Groebel, *Ann.*, 345, 155 (1906), especially p. 206.

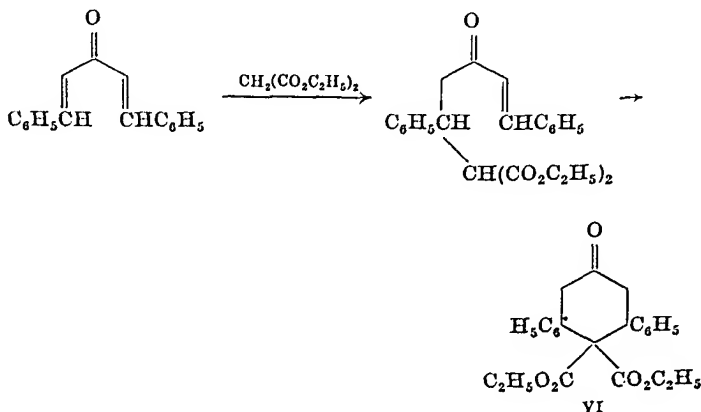
¹⁹⁵ Vorlaender and Staudinger, *Ann.*, 345, 155 (1906), especially p. 217.

and potassium hydroxide in ethanol.¹⁹⁷ This is in contradiction to the behavior of diethyl cinnamylidenemalonate (see p. 501), which undergoes 1,6 condensation. The adduct III from cinnamylideneacetophenone and acetophenone is accompanied by a product whose formation involves two moles of acetophenone. Condensation of cinnamylideneacetophenone with ethyl acetoacetate gave a substance $C_{28}H_{22}O_3$ of unelucidated structure.¹⁹⁸

Considerable attention has been paid to Michael condensations with doubly unsaturated ketones of the type $RCH=CHCOCH=CHR$, e.g., dibenzylideneacetone (IV)¹⁹⁸⁻²⁰⁰ and dicinnamylideneacetone (V).¹⁹⁸ The experimental material available, summarized in Table IV, shows that the two double bonds in dibenzylideneacetone undergo Michael condensation



independently of each other. If the donor contains two enolizable hydrogen atoms, there is often a secondary intramolecular step leading to a six-membered ring (VI).¹⁹⁸ Substances of the dicinnamylideneacetone type appear to undergo the Michael condensation by 1,4 (not 1,6) addition.¹⁹⁸



¹⁹⁷ Wittig and Kosack, *Ann.*, 529, 167 (1937).

¹⁹⁸ Kohler and Dewoy, *J. Am. Chem. Soc.*, 46, 1267 (1924).

¹⁹⁹ Kohler and Helmkamp, *J. Am. Chem. Soc.*, 46, 1018 (1924).

²⁰⁰ Marvel and Moore, *J. Am. Chem. Soc.*, 71, 28 (1949).

It is of interest to compare the reactivity of the double bonds in unsymmetrically substituted dibenzylidene-acetones. In dibenzylidene-acetone, chlorine in the 2, 3, or 4 position²⁰¹ or a methoxyl group in the 4 position¹⁹⁹ deactivates the neighboring double bond so that Michael reaction occurs only on the side of the unsubstituted benzene ring. The chlorine atom in α -(3- or 4-chlorobenzylidene)- β -(4'-methoxybenzylidene)-acetone causes the reaction to take place on the double bond adjacent to the chlorinated nucleus. On the other hand, a hydroxyl group in the 2 or 4 position of the benzene nucleus has a stronger activating influence than a 2-methoxy group or a chlorine atom in the 3 or 4 position.²⁰²⁻²⁰⁴

It is noteworthy as well as surprising that ethyl acetoacetate condenses with α -(4-dimethylaminobenzylidene)- β -(2-hydroxybenzylidene)acetone, in the presence of potassium hydroxide as catalyst on the dimethylamino group side, whereas ethyl cyanoacetate with sodium hydroxide as catalyst adds to the side of the 2-hydroxyphenyl radical.²⁰⁵ The same difference is evident in two other cases listed in Table IV.

Heterocyclic α,β -Ethylenic Ketones (Tables V, VI). In view of the aromatic character of the furan system, α,β -ethylenic ketones containing the furyl group should behave like their phenyl analogs^{121, 206-210}. This expectation is borne out by the examples in Table V. A characteristic difference, however, is the fact that almost no secondary cyclization or isomerization reactions take place. Table V also includes a few heterocyclic compounds not derived from furan.

Table VI lists a number of other heterocyclic α,β -ethylenic ketones, mostly of the acylcoumarin type.²¹¹⁻²¹³ Several reactions carried out with 2-(*p*-methoxybenzylidene)-4,5-benzo-2,3-dihydrofuran-3-one^{214, 214a} and γ -pyrone are included.²¹⁵ The reaction of γ -pyrone and diethyl malonate is somewhat complicated, but it can be assumed that the first step is a Michael condensation to VII, which is followed by ring opening and

²⁰¹ Heilbron and Hill, *J. Chem. Soc.*, 1923, 2863.

²⁰² Heilbron and Forster, *J. Chem. Soc.*, 125, 2064 (1924).

²⁰³ Heilbron and Hill, *J. Chem. Soc.*, 1927, 918.

²⁰⁴ Jennings and McGookin, *J. Chem. Soc.*, 1934, 1741.

²⁰⁵ Heilbron, Forster, and Whitworth, *J. Chem. Soc.*, 127, 2159 (1925).

²⁰⁶ Peak and Robinson, *J. Chem. Soc.*, 1937, 1581.

²⁰⁷ Andrews and Connor, *J. Am. Chem. Soc.*, 57, 895 (1935).

²⁰⁸ Drake and Gilbert, *J. Am. Chem. Soc.*, 52, 4965 (1930).

²⁰⁹ Klotzel, *J. Am. Chem. Soc.*, 69, 2271 (1947).

²¹⁰ Turner, *J. Am. Chem. Soc.*, 73, 1234 (1951).

²¹¹ Koelsch and Sundet, *J. Am. Chem. Soc.*, 72, 1661 (1950).

²¹² Koelsch and Sundet, *J. Am. Chem. Soc.*, 72, 1844 (1950).

²¹³ Sastri and Seshadri, *Proc. Indian Acad. Sci.*, 16A, 29 (1942) [*C.A.*, 37, 860 (1943)].

²¹⁴ Panse, Shah, and Wheeler, *J. Indian Chem. Soc.*, 18, 453 (1941) [*C.A.*, 36, 4507 (1942)].

^{214a} Panse, Shah, and Wheeler, *J. Univ. Bombay*, 10, Part 3, 83 (1941) [*C.A.*, 36, 4507

(1942)].

²¹⁵ R. B. Woodward, private communication.

recyclization. Elimination of one of the carbethoxyl groups makes possible the aromatization to form VIII.

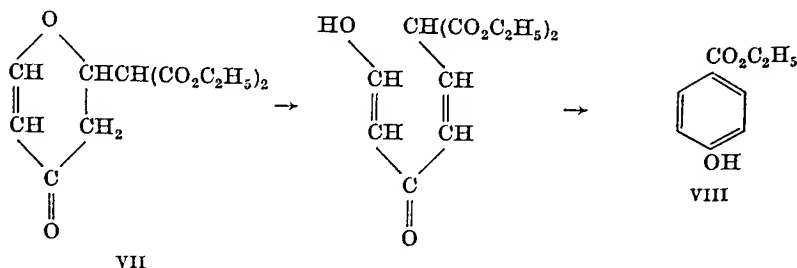
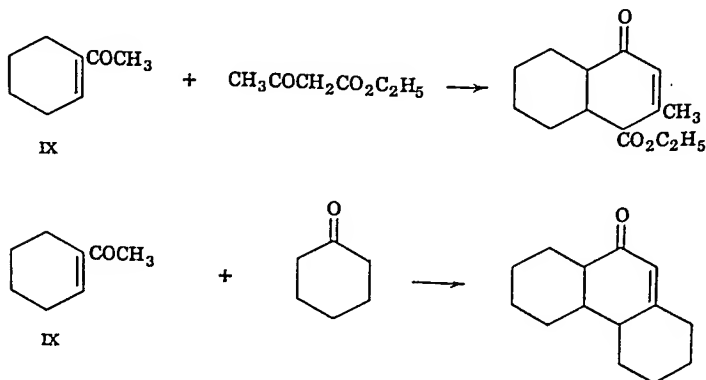


Table VI also includes the Michael condensation between rhodanine and alkylidenerhodanines. In this reaction, α, α -bis-(2-thio-4-ketotetrahydro-5-thiazolyl)alkanes are formed from rhodanine and aliphatic aldehydes.²¹⁶

Cycloalkenones and Acyl Cycloalkenes (Table VII). The Michael condensations of cycloalkenones and 1-acylcycloalkenes have been listed in a separate table (Table VII) in view of the importance of the products in the synthesis of hydroaromatic polycyclic substances related to the steroids and steroidal alkaloids.

The adducts obtained from acetylcycloalkenes^{93-99, 216-218} undergo intramolecular condensation to polycyclic ring systems, as exemplified in the accompanying reactions of 1-acetylcyclohexene (IX).^{93, 98}

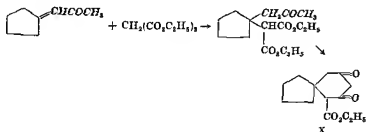


²¹⁶ Bradsher, Brown, and Grantham, *J. Am. Chem. Soc.*, **73**, 5377 (1951).

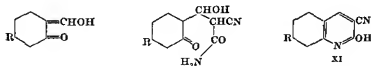
²¹⁷ Hawthorne and Robinson, *J. Chem. Soc.*, 1938, 763.

²¹⁸ Hewett, *J. Chem. Soc.*, 1938, 50.

Table VII further includes some cases in which cycloalkylideneacetones have been subjected to the Michael condensation²¹⁹⁻²²³ Here, too, cyclization of the primary adduct is spontaneous as shown by the formation of X.²²¹ As in many other reactions, the remaining carboxyl group is often eliminated in the process.



Michael condensations with hydroxymethylene- or alkoxymethylene-cycloalkanones lead to interesting cyclic products. The product, e.g., from 2-hydroxymethylenecyclohexanone and cyanoacetamide (in the presence of piperidine or diethylamine),²²⁴ eliminates water between the amide group and the carbonyl group of the cyclohexanone. The hydroxyl of the hydroxymethylene group is also eliminated as water, yielding XI ($\text{R} = \text{H}, \text{CH}_3$)



The dimerization of piperitone²²⁵ (XII) appears to be a special case of Michael condensation. The methyl group of one molecule provides the hydrogen for the saturation of the second, the first molecule behaves, therefore, as a vinylog of a methyl ketone and does not utilize the existing hydrogen in the ortho position, perhaps due to steric inhibition by the isopropyl group. Two stereoisomers are formed. The structure of the dimeride of piperitone, which is stabilized by hydrogen bond formation

²¹⁹ Kandiah, *J. Chem. Soc.*, 1931, 952.

²²⁰ Kon and Thakur, *J. Chem. Soc.*, 1930, 2317.

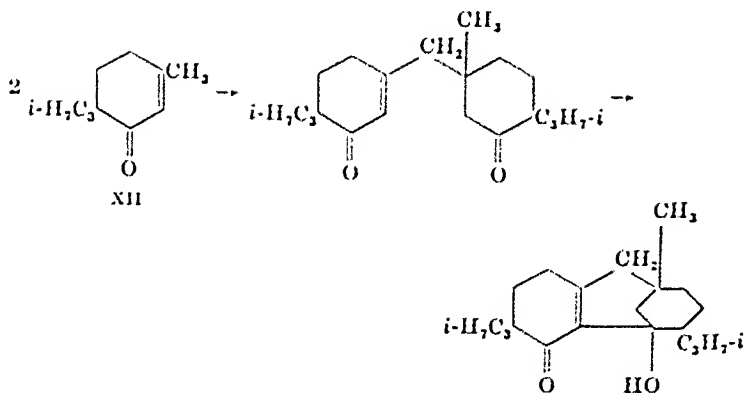
²²¹ Norris and Thorpe, *J. Chem. Soc.*, 119, 1199 (1921).

²²² Thakur, *J. Chem. Soc.*, 1932, 2147.

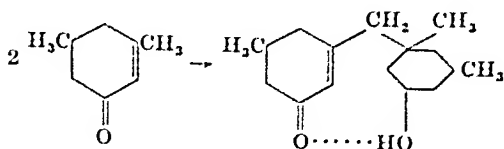
²²³ Thakur, *J. Chem. Soc.*, 1932, 2157.

²²⁴ Sen-Gupta, *J. Chem. Soc.*, 107, 1347 (1915).

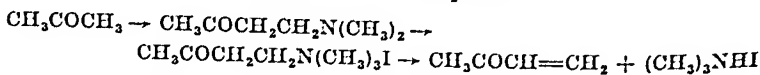
²²⁵ Taylor, *Chemistry & Industry*, 1954, 252. Cf. Cole, *ibid.*, 1954, 661.



between the carbonyl and the hydroxyl groups,²²⁶ has been indicated by analogy with evidence obtained by degradation of the dimeride of 3,5-dimethyl-2-cyclohexen-1-one.²²⁷



Robinson's Modification of the Michael Condensation (Table VIII). The use of a masked form of the α,β -ethylenic carbonyl compound, which produces the latter *in situ*, is of practical importance with sensitive ketones and in condensations requiring stringent experimental conditions. Although saturated β -chloroketones had had some use as precursors of the corresponding α,β -ethylenic ketones,²²⁸ Robinson and his co-workers^{98,229-231} introduced the use of β -dialkylaminoketones or their quaternary salts; these decompose gradually into a dialkylamine or trialkylammonium salt and the desired α,β -ethylenic ketone. These starting materials are readily accessible by appropriate Mannich reactions²³² of saturated ketones and, if necessary, subsequent quaternization as shown in the accompanying reaction sequence.



²²⁶ Briggs and Colebrook, *Chemistry & Industry*, 1955, 200.

²²⁷ Ayer and Taylor, *J. Chem. Soc.*, 1955, 2227.

²²⁸ Allen and Bell, *Can. J. Research*, 11, 40 (1934) [*C.A.*, 29, 150 (1935)].

²²⁹ du Feu, McQuillin, and Robinson, *J. Chem. Soc.*, 1937, 53.

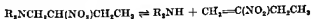
²³⁰ McQuillin and Robinson, *J. Chem. Soc.*, 1938, 1097.

²³¹ McQuillin and Robinson, *J. Chem. Soc.*, 1941, 586.

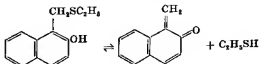
²³² Blicke, in Adams, *Organic Reactions*, Vol. 1, Chapter 10, John Wiley & Sons, 1942.

Although these reactions are included here (Table VIII) among Michael condensations, it has not been certain that they proceed by way of the α,β -ethylenic ketone as an intermediate²³³ A recent study of these reactions has led to the conclusion that the olefinic intermediate, as outlined by Robinson, occurs whenever there is a hydrogen atom on the carbon atom beta to the nitrogen *

The scope of Robinson's modification of the Michael reaction has been widened by the observation²⁵¹ that 1-dialkylamino-2-nitroalkanes (the Mannich bases of nitroalkanes) can replace the corresponding nitroolefins in Michael condensations.



Another variant is the use of the alkylthio instead of the dialkylamino group. Thus, 1-ethylthiomethyl-2-naphthol reacts as the 1-methylene derivative of the keto form of 2-naphthol.¹⁵⁵



¹⁵⁵ Brewster and Ehel, in Adams, *Organic Reactions*, Vol 7, Chapter 3, John Wiley & Sons, 1953.

* Note, however, that Bradford and co-workers²³⁴ have observed differences of reaction in cyanoethylation with β diethylaminoethyl cyanide methiodide as compared with cyanoethylation with acrylonitrile, and have assumed that the positive ion $NCCH_2CH_3^+$ is the intermediate. This explanation suggests the relation of the Michael condensation to reactions of typical Michael donors with gramine (β diethylaminoethylindole) and its derivatives²³⁵⁻²⁴⁰

²³⁴ Bradford, Meek, Turnbull, and Wilson, *Chemistry & Industry*, 1951, 839.

²³⁵ Ehel and Murphy, *J. Am. Chem. Soc.*, 75, 3589 (1953)

²³⁶ Dornow and Thies, *Ann.*, 581, 219 (1953)

²³⁷ Holland and Naylor, *J. Chem. Soc.*, 1953, 290

²³⁸ Gray, *J. Am. Chem. Soc.*, 75, 1252 (1953).

²³⁹ Kissman and Witkop, *J. Am. Chem. Soc.*, 75, 1967 (1953)

²⁴⁰ Atkinson, Poppeledorf, and Williams, *J. Chem. Soc.*, 1953, 580.

²⁴¹ Jones and Kornfeld, U S pat. 2,621,187 [C.A., 47, 10557 (1953)].

²⁴² Kutscher and Klamerth, *Chem. Ber.*, 86, 352 (1953)

²⁴³ Brewster and Ehel, in Adams, *Organic Reactions*, Vol 7, p. 99, John Wiley & Sons,

1953

²⁴⁴ Thiesing, *Chem. Ber.*, 87, 692 (1954)

²⁴⁵ Atkinson, *J. Chem. Soc.*, 1954, 1329

²⁴⁶ Hellmann, Hallmann, and Langens, *Chem. Ber.*, 86, 1346 (1953).

²⁴⁷ Hardegger and Corrodi, *Helv. Chim. Acta*, 38, 468 (1955).

²⁴⁸ Albertson, Archer, and Suter, *J. Am. Chem. Soc.*, 66, 500 (1944)

²⁴⁹ Snyder and Smith, *J. Am. Chem. Soc.*, 66, 330 (1944).

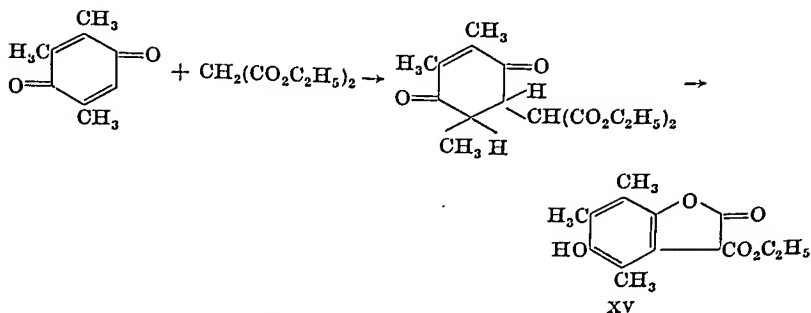
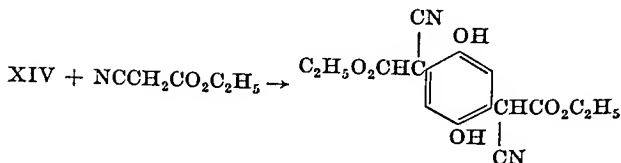
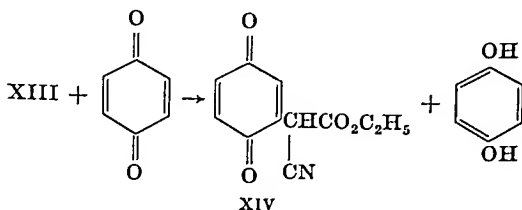
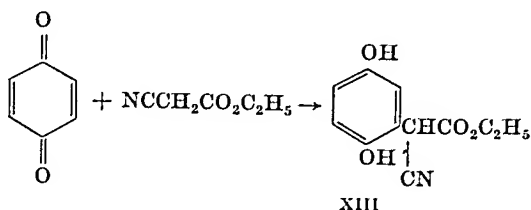
²⁵⁰ Lyttle and Weusliat, *J. Am. Chem. Soc.*, 69, 2118 (1947)

²⁵¹ Hegedus, *Helv. Chim. Acta*, 29, 1499 (1946).

²⁵² Shoemaker and Keown, *J. Am. Chem. Soc.*, 76, 6374 (1954).

***p*-Quinones and Derivatives (Table IX).** As in many other reactions, e.g., the Diels-Alder synthesis, *p*-quinones behave in the Michael condensation as α,β -ethylenic ketones. However, although the enols formed in the Michael condensation of most α,β -ethylenic ketones ketonize spontaneously, the enols formed from quinones are hydroquinones and are stable.

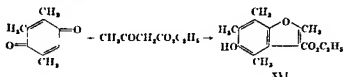
Certain of the hydroquinone products are dehydrogenated *in situ* by an excess of the original quinone, so that the newly formed quinone can undergo a second Michael condensation.²⁵²



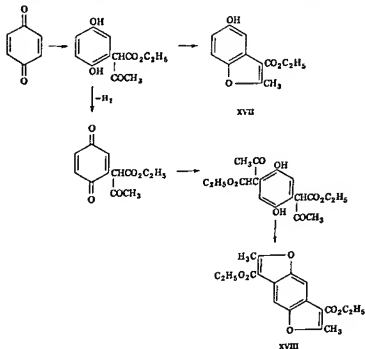
²⁵² Wood, Colburn, Jr., Cox, and Garland, *J. Am. Chem. Soc.*, **66**, 1540 (1944).

Other hydroquinones undergo cyclization involving the hydroxyl group of the hydroquinone and leading to condensed heterocyclic ring systems. As example is the formation of the lactone XV shown on p. 224.²⁵²

In other cases not only isocoumarones are formed, but also coumarin derivatives such as XVI.²⁵⁴ When zinc chloride is used to catalyze the



reaction of *p*-benzoquinone and ethyl acetoacetate, either a mono (XVII) or bis derivative (XVIII) can be formed.²⁵⁵⁻²⁵⁷ Cyclization also takes place



²⁵² Smith and Preckard, *J. Org. Chem.*, **4**, 342 (1939)

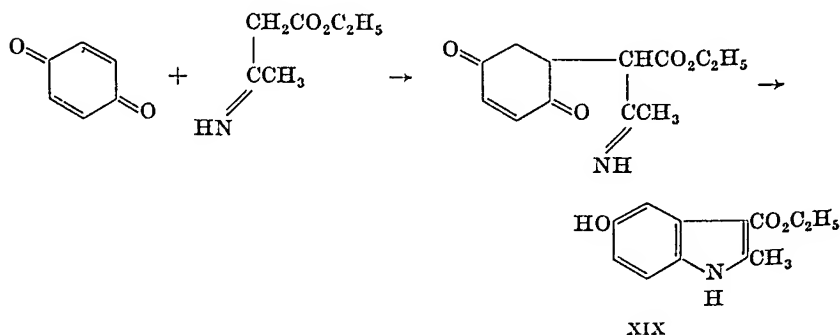
²⁵⁴ Smith and Boyack, *J. Am. Chem. Soc.*, **70**, 2690 (1948)

²⁵⁵ Pechmann, *Ber.*, **21**, 3005 (1888)

²⁵⁶ Ikuta, *J. prakt. Chem.*, [2], **45**, 78 (1892)

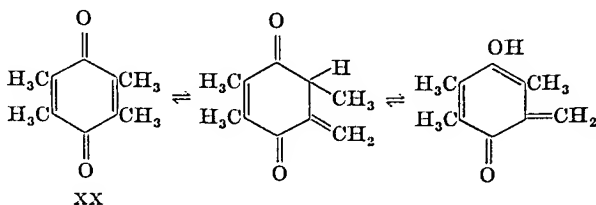
²⁵⁷ Graebe and Levy, *Ann.*, **283**, 245 (1894)

when benzoquinone reacts with the imine of ethyl acetoacetate (ethyl β -aminocrotonate). In acetone or anhydrous ethanol as solvent, 2-methyl-3-carbethoxy-5-hydroxyindole (XIX) is formed.²⁵⁸ In the same way,



N-phenyl-2-methyl-3-carbethoxy-5-hydroxyindole was obtained with ethyl β -anilinoacrylate, and the corresponding N-carbethoxymethyl compound from ethyl β -(carbethoxymethylamino)acrylate.

Ordinarily only an unsubstituted carbon atom of the quinone ring is attacked by a donor anion, possibly for steric reasons. Thus, trisubstituted quinones undergo only mono condensation.^{254,259,260} However, it



is possible for a tetrasubstituted quinone to participate in the Michael condensation.²⁶¹⁻²⁶³ A substance like duroquinone (XX) presumably reacts in a tautomeric form (considered to be the intermediate in the "dimerization" of this quinone),²⁶⁴ which is evidently much freer of steric hindrance than the normal form.

In one instance, a methylene quinone (1-methylene-1,2-naphthoquinone, XXI) has been shown to undergo the Michael reaction with diethyl

²⁵⁸ Nenitzescu, *Bul. Soc. Chim. România*, **11**, 37 (1929) [*C.A.*, **24**, 110 (1930)].

²⁵⁹ Smith and Kaiser, *J. Am. Chem. Soc.*, **62**, 133 (1940).

²⁶⁰ Smith and King, *J. Am. Chem. Soc.*, **65**, 441 (1943).

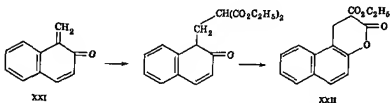
²⁶¹ Smith and Dobrovolny, *J. Am. Chem. Soc.*, **48**, 1893 (1926).

²⁶² Smith and Kaiser, *J. Am. Chem. Soc.*, **62**, 138 (1940).

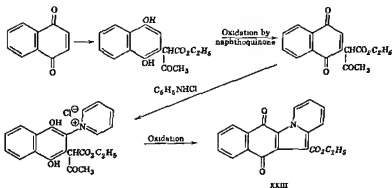
²⁶³ Smith and Tenenbaum, *J. Am. Chem. Soc.*, **59**, 667 (1937).

²⁶⁴ Smith, Tess, and Ulliot, *J. Am. Chem. Soc.*, **66**, 1320 (1944).

malonate, though in small yield. In this case, too, cyclization occurred and ethyl 5,6-benzo-3,4-dihydrocoumarin-3-carboxylate (XXII) was formed.²⁶⁵



A complicated modification of the Michael reaction of *p*-quinones has been observed to result from condensation of 1,4-naphthoquinone (cf. ref. 261) with ethyl acetoacetate in the presence of pyridine and pyridinium hydrochloride,²⁶⁶ cf. ref. 267. The final product had lost the acetyl group of the acetoacetate molecule; the same product (1-carbethoxy-2,3-phthaloylpyrrocoline, XXIII) was therefore obtained when ethyl benzoylacetate was employed. The reaction has been formulated as shown.



The complexity of this sequence explains the low yield (14%) as well as the fact that also 2-bromo- and 2,3-dichloro-naphthoquinone and 1,4-naphthoquinone-2-sulfonate give the same product, with loss of the polar

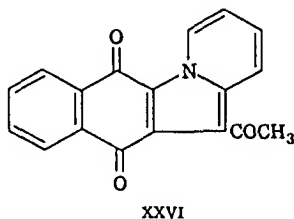
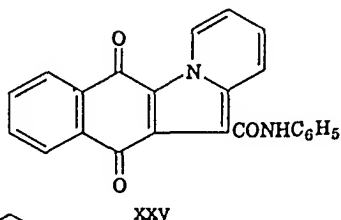
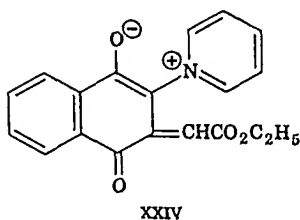
²⁶⁵ Smith and Horner, Jr., *J. Am. Chem. Soc.*, **60**, 576 (1938).

²⁶⁶ Pratt, Luckenbaugh, and Erickson, *J. Org. Chem.*, **19**, 176 (1954).

²⁶⁷ Pratt and Boehme, *J. Am. Chem. Soc.*, **73**, 444 (1951). Isoquinoline shows a reactivity comparable with that of pyridine. Quinoline, however, is relatively unreactive and the products described in ref. 266 as derived from quinoline have been shown to have been formed from isoquinoline present in the quinoline used. Pratt, Rice, and Luckenbaugh, *J. Am. Chem. Soc.*, **79**, 1212 (1957).

substituents.²⁶⁸ According to Suryanarayana and Tilak,²⁶⁹ 2,3-dichloronaphthoquinone also yields the same compound (XXIII) when condensed with diethyl malonate or ethyl benzoylacetate. The Indian authors assigned to it, originally, the formula XXIV, but withdrew it later in favor of XXIII.²⁷⁰⁻²⁷³

They further observed, in the condensation of 2,3-dichloro-1,4-naphthoquinone with acetoacetanilide in pyridine, that the ultimate partial degradation of the side chain involved *either* the acetyl *or* the anilide group, thus leading both to XXV and XXVI. Compound



XXVI is also obtained when acetoaceto-*o*-chloroanilide, -*o*-toluide, or 2-(acetoacetamido)-6-ethoxybenzothiazole is employed instead of the unsubstituted anilide.

An analogous reaction was observed when ethyl acetoacetate in pyridine solution was condensed with chloranil or 2,6-dichloroquinone, leading to a mixture of XXVIIA and XXVIIB. The structure of XXVIIA was proved by its synthesis from tetraethyl 2,5-dichloroquinone-3,6-dimalonate and ethyl acetoacetate in pyridine solution.

²⁶⁸ Michel, *Ber.*, **33**, 2402 (1900).

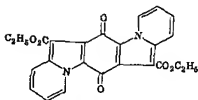
²⁶⁹ Suryanarayana and Tilak, *Proc. Indian Acad. Sci.*, **39A**, 185 (1954) [*C.A.*, **49**, 12411 (1955)].

²⁷⁰ Suryanarayana and Tilak, *Proc. Indian Acad. Sci.*, **38A**, 534 (1953) [*C.A.*, **49**, 2396 (1955)].

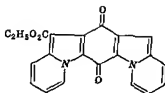
²⁷¹ Suryanarayana and Tilak, *Current Sci. India*, **22**, 171 (1953) [*C.A.*, **48**, 14212 (1954)].

²⁷² Acharya, Tilak, and Venkiteswaran, *J. Sci. Ind. Research India*, **14B**, 250 (1955) [*C.A.*, **50**, 15531 (1956)].

²⁷³ Acharya, Suryanarayana, and Tilak, *J. Sci. Ind. Research India*, **14B**, 394 (1955) [*C.A.*, **50**, 12971 (1956)].

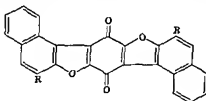


XXVIIA



XXVIIIB

Chloranil enters also into Michael reactions with β -naphthol or 2-hydroxy-3 naphthamide. These donors react in their tautomeric keto forms, as in several other instances (see p 211), and cause the loss of the halogen atoms, leading to compounds of the following type



(R = H, CONHC₂H₅)

Acrylonitrile, Other α,β -Unsaturated Nitriles, and Their Amides (Tables X, XI, and XIIA). Acrylonitrile has been used as an acceptor in Michael synthesis more widely than any other derivative of α,β -ethylenic acids. The reaction with acrylonitrile has not only been used for preparative purposes, but it has become a tool for testing organic molecules for enolizable hydrogen atoms. The literature is summarized in Table X, which also brings up to date an earlier review of the cyanoethylation reaction.²⁷⁴

Some interesting generalizations emerge from Table X. In aliphatic methyl ketones, a methine group adjacent to the carbonyl is more reactive than a methylene group, and a methylene group is more reactive than a methyl group.²⁷⁵⁻²⁷⁷ In cyclohexanone and 2-substituted cyclohexanones, hydrogen in the 2 position reacts first with acrylonitrile;^{114,275,276,279} when no more labile hydrogen remains at the 2 position, the 6 position is

²⁷⁴ Brunson, in Adams, *Organic Reactions*, Vol. 5, p. 79, John Wiley & Sons, 1949. See also U.S. pat. 2,396,736 (C. 4, 40, 7234 (1946)).

²⁷⁵ Barkley and Levine, *J. Am. Chem. Soc.*, 72, 3699 (1950).

²⁷⁶ Campbell, Carter, and Slater, *J. Chem. Soc.*, 1948, 1741.

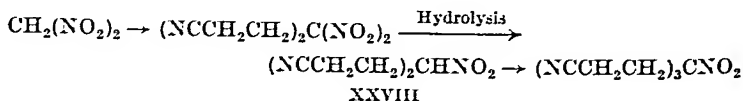
²⁷⁷ Zellars and Levine, *J. Org. Chem.*, 13, 911 (1948).

²⁷⁸ Brunson and Niederhäuser, U.S. pat. 2,437,905 (C. 4, 42, 4196 (1948)).

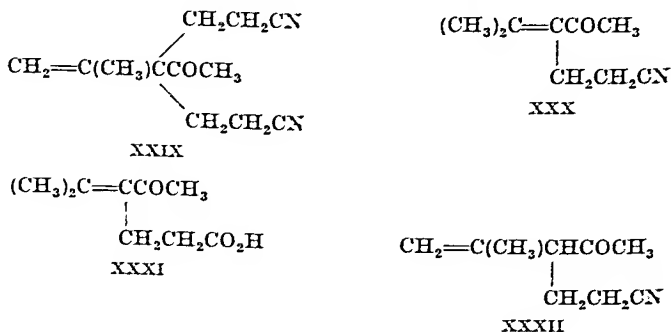
²⁷⁹ Brunson and Riener, *J. Am. Chem. Soc.*, 70, 214 (1948).

attacked by the nitrile.^{275,279} In aryl methyl ketones, all three hydrogen atoms of the methyl group react successively with acrylonitrile.²⁷⁷

Nitromethane and nitroethane are reported to give varying yields in the reaction with acrylonitrile.^{117,280-282} Dinitromethane, on the other hand, readily gives bis(cyanoethyl)dinitromethane, which loses one nitro group, and the scission product reacts with a third molecule of acrylonitrile to yield tris(cyanoethyl)nitromethane.⁸⁰⁹



In some α,β -ethylenic carbonyl and carboxyl compounds, the inherent possibility of tautomerization to the β,γ -unsaturated forms is enhanced by the reaction with acrylonitrile. From mesityl oxide, for example, a mono and a bis adduct are obtained;^{283,284} cf. ref. 764. For the latter, the formula XXIX has been established by degradation. For the former, Bruson and Riener have proposed the α,β -unsaturated structure XXX because of the formation of XXXI by hydrolysis. The evidence does



not exclude the possibility, however, that during hydrolysis the double bond shifts into the α,β position and that the correct structure is the one shown in XXXII. In any event, XXXII undoubtedly represents the structure of the primary product of the interaction between acrylonitrile and mesityl oxide.

Revising a previous statement²⁸³ on the reaction of isophorone with acrylonitrile, Bruson and Riener have obtained mono-, bis-, and

²⁸⁰ Thurston, Can. pat. 443,713 [*C.A.*, 42, 205 (1948)].

²⁸¹ Wulff, Hopff, and Wiest, Ger. pat. 728,531 [*C.A.*, 38, 376 (1944)].

²⁸² Bruson and Riener, *J. Am. Chem. Soc.*, 65, 23 (1943).

²⁸³ Bruson and Riener, *J. Am. Chem. Soc.*, 64, 2850 (1942).

²⁸⁴ Bruson and Riener, *J. Am. Chem. Soc.*, 66, 56 (1944).

tris-cyanoethyl derivatives (XXXIII to XXXV) of isophorone, to which they assigned the following structures ($R = CH_2CH_2CN$)²⁶⁵



XXXIII



XXIV



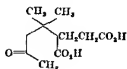
XXXV



XXXVI



XXXVII



XXXVIII

However, it has been shown²⁶⁶ that the mono derivative is XXXVI, as it could be ozonized to yield 3,3-dimethyl-5-ketohexanoic acid (XXXVII) (after hydrolysis of the nitrile group), whereas XXXIII should have given XXXVIII. As in the case of mesityl oxide (p. 230), the tautomeric



XXXIX



XL

form (XXXIX) of isophorone undergoes reaction, the primary product XL then isomerizes to an α,β -unsaturated ketone. The infrared spectra of the bis and tris products reported by Bruson and Riener²⁶⁵ suggest the following structures for the mono-, di-, and tri-cyanoethylated products, respectively

 $\lambda = 6.05$  $\lambda \sim 5.90$  $\lambda = 5.90$

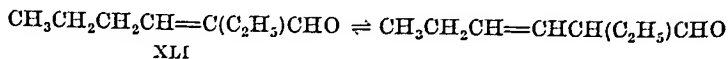
The alkylation of isophorone takes place in an analogous manner.²⁶⁷

²⁶⁵ Bruson and Riener, *J. Am. Chem. Soc.*, **75**, 3585 (1953)

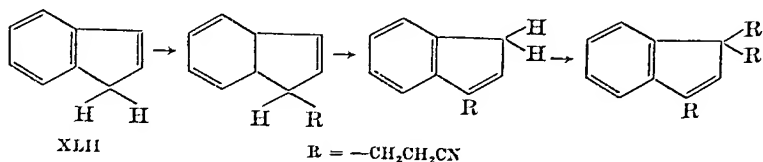
²⁶⁶ Julia, *Compt. rend.*, **237**, 913 (1953)

²⁶⁷ Comua, *Bull. soc. chim. France*, 1954, 820

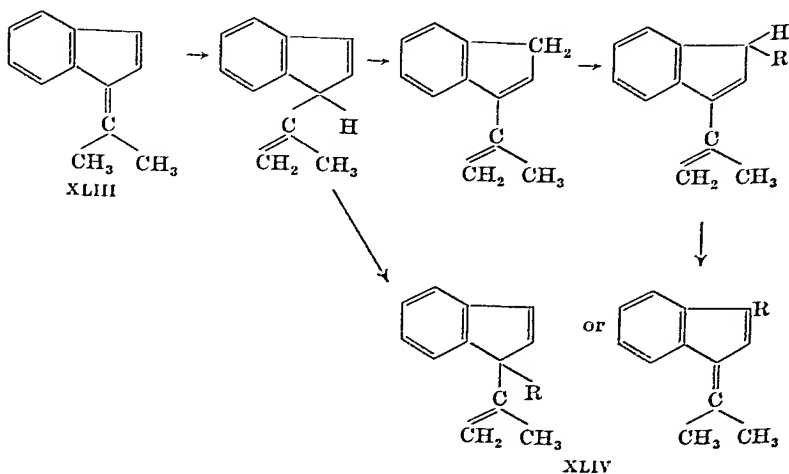
2-Ethyl-2-hexenal (XLI) also reacts in the β,γ -isomeric form with crotononitrile and β,β -dimethylacrylonitrile.



An interesting point emerges from the behavior of compounds such as indene (XLII),²⁸⁸ which gives a tris(cyanoethyl) derivative. One has to assume that the primary products rearrange to give a new reactive methylene group. In a similar fashion, cyclopentadiene gives a hexacyanoethyl derivative.

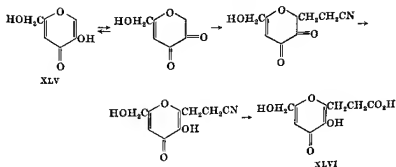


In the reaction of dimethylbenzofulvene (XLIII), it has been supposed that an isomerization precedes the reaction.



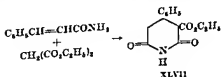
Kojic acid (XLV) provides an instance in which an enolic hydroxyl group reacts in the tautomeric keto form;¹⁷⁰ after hydrolysis the product is a 6-propionic acid derivative (XLVI) of kojic acid:

²⁸⁸ Bruson, *J. Am. Chem. Soc.*, **64**, 2457 (1942).



Considerably less work has been done on the Michael condensation with other unsaturated nitriles. The available data, collected in Table XI deal mainly with cinnamonnitrile,^{27,289,290} and allyl cyanide,^{27,77,217,291} isomerized to crotononitrile by the alkaline reagents that catalyze the Michael condensation. Table XI also includes some data on 1-cyanobutadiene^{91,292,293} In contradistinction to $\alpha,\beta,\gamma,\delta$ -diethylenic ketones (see p 217), the Michael condensation of 1-cyanobutadiene with nitroalkanes takes place in the 1,6 positions, yielding β,γ -unsaturated nitriles²⁹³

α,β -Unsaturated amides could be expected to react in the same manner as the nitriles. Acrylamide adds, in the presence of benzyltrimethylammonium hydroxide, one molecule of 2-nitropropane,²⁹⁴ and cinnamamide condenses with diethyl sodiomalonate to give the normal 1:1 adduct which cyclizes to yield ethyl 2,6-diketo-4-phenylpiperidine-3-carboxylate (XLVII).^{294a} However, in the reactions studied (Table XIId) acrylamide appears to offer no particular advantage for synthesis.²⁹⁵



¹⁰⁰ Campbell and Fairfull, *J. Chem. Soc.*, 1949, 1239.
¹⁰¹ *J. Chem. Soc.*, 85, 2459 (1943).

100 Campbell and Fairfull, *J. Chem. Soc.*, 201 (1943)
101 Koelsch, *J. Am. Chem. Soc.*, 65, 2439 (1943)

210 Koelsch, J. Am. Chem. Soc., 1949, 71, 5212
211 Tucker, J. Chem. Soc., 1949, 2152

in Tucker, *J. Chem Soc*, 1949, 2182

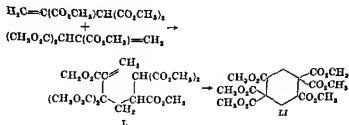
100 Branson, U.S. pat. 2,484,683 [C.A., 49, 5561 (1955)].

¹⁹⁴ Bruzon, U.S. pat. 2,370,142 [C.A., 39, 3544 (1945)]

1960 Herrmann and Vorlaender, *Chem. Zentr.*, 1960, 1037

194. Lind and Ginsburg, *J. Chem. Soc.*, 1953, 4137

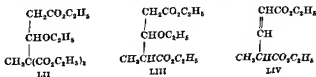
Michael condensations. The first yields the open-chain ester L, whereas the second is intramolecular and yields the cyclic product LI.³⁰³



The addition of ethyl 5-methylcyclopentanone-2-carboxylate to ethyl crotonate involves the α -hydrogen atom in the 2 position, and not in the 5 position as erroneously stated in the abstract literature^{304,305}

The Michael reaction is not involved in the condensation of ethyl acetoacetate and diethyl acetone-1,3-dicarboxylate to diethyl 3,5-dihydroxytoluene-2,4-dicarboxylate³⁰⁶

Table XIII is devoted to reactions of β -hydroxy-, β -ethoxy-, and β -amino- α,β -ethylene esters. These reactions are generally accompanied by the elimination of the β substituent (as water, alcohol, or ammonia, respectively). For example, when ethyl β -ethoxyacrylate is condensed with diethyl methylmalonate under the catalytic influence of benzyltrimethylammonium ethoxide, the expected triester LII not only undergoes ethanolysis to diethyl carbonate and the diester LIII but the diester decomposes further to give ethanol and the unsaturated ester LIV.³⁰⁷



The behavior of diethyl 2-ethoxyethylene-1,1-dicarboxylate LV is very similar.³⁰⁸⁻³¹⁰ With nitromethane and secondary bases the ester LV

³⁰³ Baker, *J. Chem. Soc.*, 1935, 188.

³⁰⁴ Sen Gupta, Chakraborty, and Bhattacharayya, *J. Indian Chem. Soc.*, 24, 249 (1947) [*C.A.*, 43, 2584 (1949)].

³⁰⁵ Private communication from Dr. B. K. Bhattacharayya.

³⁰⁶ Koller and Krekauer, *Monatsh.*, 53-54, 931 (1929).

³⁰⁷ Croxall and Fegley, *J. Am. Chem. Soc.*, 72, 970 (1950).

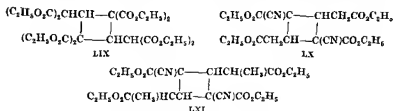
³⁰⁸ Menon, *J. Chem. Soc.*, 1935, 1061.

³⁰⁹ Menon, *J. Chem. Soc.*, 1938, 1775.

³¹⁰ Simonsen, *J. Chem. Soc.*, 93, 1022 (1908).

mesaconate, this is the only example of the use of this *trans* compound as an acceptor in the Michael condensation³¹⁷

In the Michael condensation of esters of polycarboxylic acids, two tendencies are apparent. First, the highly substituted reaction products tend to dissociate into simpler substances by elimination of some smaller molecules, such as ethanol or diethyl malonate, with formation of a double bond^{318,319-321}. Second, those adducts containing both an enolizable hydrogen atom and a suitable acceptor structure undergo an intramolecular Michael condensation with the formation of a six-membered ring. Tetraethyl propylene-1,1,3,3-tetracarboxylate is reported to lead, under the influence of piperidine or sodium ethoxide, to the cyclobutane derivative LIX,³²¹⁻³²³ and piperidine converts diethyl



3-cyanopropylene-1,3-dicarboxylate and diethyl 4-cyanobutylene-2,4-dicarboxylate into the cyclobutanes LX and LXI, respectively^{322,323}. However, reaction of diethyl acetylenedicarboxylate with tetraethyl ethane 1,1,2,2-tetracarboxylate has been recently shown^{324,325} to give not a cyclobutane derivative but hexaethyl butene-1,1,2,2,3,4 hexacarboxylate

Table XIV summarizes our knowledge of the behavior of aliphatic dienic esters and one trienic ester in the Michael condensation. With the dienic esters, 1,6 addition predominates over 1,4 addition; with the trienic ester, 1,3 addition predominates. This, however, applies only to esters in which the polar groups are unsymmetrically distributed about the double bond, dialkyl muconates, $\text{RO}_2\text{CCH}=\text{CHCH}=\text{CHCO}_2\text{R}$, undergo 1,4 addition exclusively, giving $\text{RO}_2\text{CCH}=\text{CHCHR}'\text{CH}_2\text{CO}_2\text{R}$ ³²⁶

³¹⁷ Hope, *J. Chem. Soc.*, 101, 892 (1912)

³¹⁸ Cornforth and Robinson, *J. Chem. Soc.*, 1949, 1855

³¹⁹ Cox and McElvain, *J. Am. Chem. Soc.*, 56, 2459 (1934)

³²⁰ Cox, Kroeker and McElvain, *J. Am. Chem. Soc.*, 56, 1173 (1934)

³²¹ Guthzeit, *Ber.*, 34, 675 (1901)

³²² Ingold, Perren, and Thorpe, *J. Chem. Soc.*, 121, 1765 (1922) especially p. 1788

³²³ Verkeke, *Verlag Akad. Wetenschappen Amsterdam*, 27, 1130 (1919) [C 4, 13, 3149

(1919)]

³²⁴ Overberger and Kabaankalian, *J. Am. Chem. Soc.*, 75, 6048 (1953)

³²⁵ Reid, *Chemistry & Industry*, 1953, 846

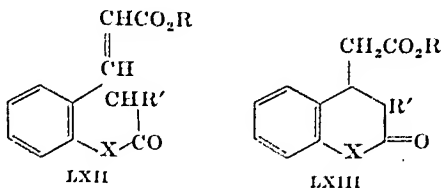
³²⁶ Farmer, *J. Chem. Soc.*, 121, 2015 (1922)

Alicyclic and Aromatic α,β -Ethylenic Esters (Tables XV and XVI). In the alicyclic series, a small number of Michael condensations have been carried out (Table XV). These proceed normally, and the only point of interest is that the reactions of ethyl cyclopentene-1-carboxylate with ethyl acetoacetate and diethyl malonate, respectively, give exclusively the *trans* form of the reaction products.⁵² As pointed out on p. 199, relatively little is known of the stereochemistry of the Michael reaction.

In the aromatic series, even fewer reactions have been studied (Table XVI). Acetophenone gives a Michael condensation with methyl and ethyl cinnamate; it is in competition, however, with a Claisen condensation between the reactants under the influence of sodium amide or sodium. Acetone undergoes with alkyl cinnamates the Claisen reaction exclusively.^{327,328}

The three dienic esters that have been studied do not give a consistent picture. In two of them 1,6 and in one 1,4 addition takes place, without any obvious difference either in the structure of the unsaturated ester or in the operating conditions.^{56,194,195,329}

Ortho-substituted aromatic α,β -ethylenic esters provide ideal structures for internal Michael condensation. If one introduces in the ortho position to the unsaturated ester group a substituent that contains an enolizable hydrogen atom at a suitable distance from the ring, a bicyclic system can be formed easily. This possibility has been utilized with substances of the general formula LXII for the synthesis of bicyclic systems such as LXIII, where X = O, S, or N-alkyl. The pertinent data form the second part of Table XVI, in which an analogous case from the alicyclic series is also included.



Unsaturated Keto Esters (Table XVII). Table XVII contains the scanty material pertaining to the Michael condensation of unsaturated keto esters, in which the double bond is activated both by a keto and an ester group.^{8,120,310,330,331} It is interesting to note that in esters of the type $\text{RCOCH}=\text{CHCO}_2\text{R}'$, the keto group gives a more stable carbanion

³²⁷ Hauser, Yost, and Ringler, *J. Org. Chem.*, **14**, 261 (1949).

³²⁸ Ryan and Dunlea, *Proc. Roy. Irish Acad.*, **32B**, 1 (1913) [*Chem. Zentr.*, **1913**, II, 2039].

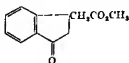
³²⁹ Kohler and Engelbrecht, *J. Am. Chem. Soc.*, **41**, 764 (1919).

³³⁰ Errera, *Ber.*, **33**, 2969, 3469 (1900).

³³¹ Palit, *J. Indian Chem. Soc.*, **14**, 354 (1937) [*C.A.*, **32**, 561 (1938)].

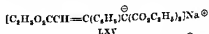
than the ester group the Michael condensation with a donor $R'H$ leads to a product of the structure $RCOCH_2CHR'CO_2R'$

Theoretically, it should be possible to effect internal Michael condensations with α -acetyl derivatives of cinnamic acid. It has, indeed, been found that methyl α -acetylcinnamate reacts with sodium methoxide, but the expected product LXIV could not be isolated in pure form.³³²

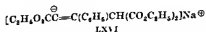


LXIV

Aromatic α,β -Acetylenic Esters (Table XVIII). In the aromatic series, as in the aliphatic, an acetylenic bond in conjunction with an ester group behaves in the Michael condensation like a double bond (Table XVIII). In certain cases, the correct formulation of the anion of the primary product of the condensation appears uncertain. It has been observed, for example, that the condensation of ethyl phenylpropiolate with diethyl malonate, using ethanolic sodium ethoxide and using sodium in benzene, lead to different anions, formulated as LXV and LXVI.^{25,26,333,334} This problem is discussed on p 186.

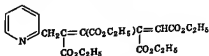


LXV

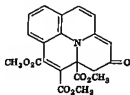


LXVI

It is often thought that the reaction between acetylenic esters and substances like 2-picoline or quinaldine is a specific case of the Michael condensation, although the components react in a 2:1 ratio. Diethyl acetylenedicarboxylate and 2-picoline yield the conjugated diene LXVII;



LXVII



LXVIII

³³² Koelech and Stephens, Jr., *J. Am. Chem. Soc.*, **72**, 2209 (1950)

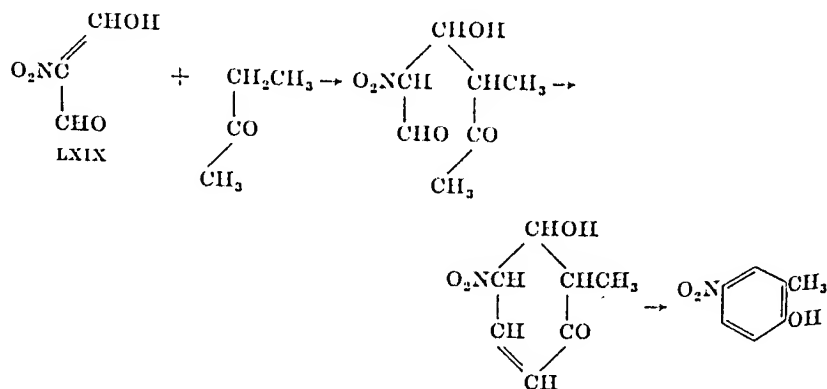
³³³ Farmer, Ghosal, and Kon, *J. Chem. Soc.*, 1936, 1804

³³⁴ Michael, *J. Org. Chem.*, **2**, 303 (1938)

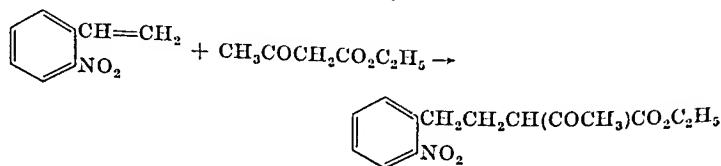
the acetylenic dimethyl ester with 2-quinaldine gives the analogous, but more complex, product LXVIII.³³³⁻³³⁷

It is known that similar dimeric forms of acetylenic compounds often occur in the Diels-Alder reaction at least as formal intermediary products.³³⁸

Olefins with Substituents Based on Hetero Atoms (N, S, P; Tables XIX, XX, XXI). A nitro group activates a double bond to which it is attached as it activates adjacent hydrogen atoms. Table XIX summarizes the Michael condensations involving α,β -ethylenic nitro compounds. Data pertaining to hydroxymethylenenitroacetaldehyde (the enolic form of nitromalondialdehyde, LXIX) are included. This



compound reacts with many donor molecules, including even aliphatic ketones, to give derivatives of 4-nitrophenol.^{111,339-343} The reaction with methyl ethyl ketone is illustrative. The activating power of the nitro group is so great that *o*- and *p*-nitrostyrene can also act as acceptors in



³³⁵ Diels, Alder, et al., *Ann.*, **498**, 16 (1932).

³³⁶ Diels and Kech, *Ann.*, **519**, 140 (1935).

³³⁷ Diels and Pistor, *Ann.*, **530**, 87 (1937).

³³⁸ Diels and Alder, *Ann.*, **498**, 16 (1932); *ibid.*, **505**, 103 (1933); *ibid.*, **510**, 87 (1934); Diels and Kock, *ibid.*, **556**, 38 (1944).

³³⁹ Hill and Torrey, Jr., *Am. Chem. J.*, **22**, 89 (1899).

³⁴⁰ Hill and Hale, *Am. Chem. J.*, **33**, 1 (1905).

³⁴¹ Hill, *Ber.*, **33**, 1241 (1900).

³⁴² Prelog and Wiesner, *Helv. Chim. Acta*, **30**, 1465 (1947).

³⁴³ Prelog, Wiesner, Ingold, and Haefliger, *Helv. Chim. Acta*, **31**, 1325 (1948).

the Michael reactions. Formally, the addition of the donor takes place in the γ, δ and ε, ζ positions of the activated unsaturated system, respectively.³⁴⁴

It appears that the S=O bond in sulfoxides and sulfones (Table XX) has sufficient double bond character to conjugate with and activate neighboring ethylenic double bonds.³⁴⁵⁻³⁵⁴ In this respect, it is recalled that 1,2-bis(arylsulfonyl)ethenes are highly active dienophiles,³⁵⁵ and that vinyl sulfones add aromatic hydrocarbons in the presence of aluminum chloride in the same manner as do α, β -unsaturated ketones.³⁵⁶ Organo-magnesium and organolithium compounds also add 1,4 to α, β -unsaturated sulfones.³⁵⁷

Table XX also includes the Michael reactions of N,N-diethylvinyl-sulfonanilide³⁵⁸ and the interesting condensations of vinyl dimethylsulfonium bromide with ethyl acetoacetate and diethyl malonate.²²

Reactions involving diethyl vinylphosphonate, $\text{CH}_2=\text{CHPO}(\text{OC}_2\text{H}_5)_2$, a newly discovered type of acceptor in the Michael reaction, are listed in Table XXI. It has already been pointed out (p. 204) that compounds containing phosphono groups have sufficiently active hydrogen atoms to serve as donors in the Michael condensation. The reaction referred to here leads to the supposition that the P=O bond, like the S=O bond, is able to form a conjugated system with an adjacent ethylenic linkage.

2- and 4-Vinylpyridines (Table XXI). Although practically no work appears to have been done on the ability of the open-chain system $\text{C}=\text{C}-\text{C}=\text{N}$ to undergo Michael condensations (see p. 207), the behavior of 2- and 4-vinylpyridine shows that, at least under certain conditions, this system gives typical Michael products. The reactions investigated appear in Table XXI.³⁵⁹

³⁴⁴ Dale and Strobel, *J. Am. Chem. Soc.*, **76**, 6172 (1954).

³⁴⁵ Samuel, *J. Chem. Physics*, **12**, 380 (1944), *ibid.*, **13**, 672 (1945); Bergmann and Tschudnowsky, *Ber.*, **65**, 457 (1932); Lister and Sutton, *Trans. Faraday Soc.*, **35**, 495 (1939). See, however, Arndt and Eistert, *Ber.*, **74**, 423 (1941).

³⁴⁶ Koch, *J. Chem. Soc.*, 1950, 2892.

³⁴⁷ Karrer, Antia, and Schwyzler, *Helv. Chim. Acta*, **34**, 1392 (1951).

³⁴⁸ Varsanyi and Ledik, *Acta Chim. Acad. Sci. Hung.*, **3**, 243 (1953) [*C.A.*, **47**, 11000 (1953)].

³⁴⁹ Kloosterziel and Backer, *Rec. trav. chim.*, **72**, 185 (1953).

³⁵⁰ Zollinger, Buechler, and Wittwer, *Helv. Chim. Acta*, **36**, 1711 (1953).

³⁵¹ Bordwell and Andersen, *J. Am. Chem. Soc.*, **75**, 6019 (1953).

³⁵² Jaffé, *J. Phys. Chem.*, **58**, 185 (1954).

³⁵³ Price and Morita, *J. Am. Chem. Soc.*, **75**, 4747 (1953).

³⁵⁴ Price and Gilis, *J. Am. Chem. Soc.*, **75**, 4750 (1953).

³⁵⁵ Truce and McManis, *J. Am. Chem. Soc.*, **75**, 1672 (1953).

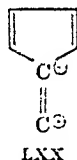
³⁵⁶ Truce, Simms, and Hill, *J. Am. Chem. Soc.*, **75**, 5411 (1953).

³⁵⁷ Potter, *J. Am. Chem. Soc.*, **76**, 5472 (1954).

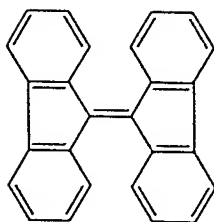
³⁵⁸ Buess and Jones, *J. Am. Chem. Soc.*, **76**, 5558 (1954).

³⁵⁹ For the addition of enolizable hydrogen compounds to the $\text{C}=\text{N}$ double bond itself, see Lazzareschi³⁵⁹ and Philpott and Jones.³⁶¹

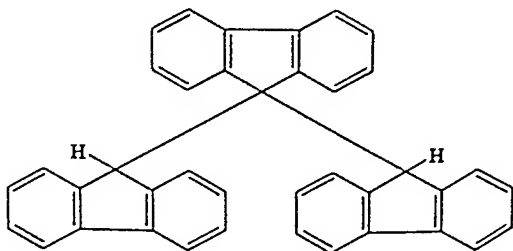
Fulvenes. Calculations as well as physical and chemical evidence have shown that the fulvenes, represented by the formula LXX, possess a polar double bond.^{360,361} It is, therefore, not surprising that fulvenes are



also acceptors in the Michael condensation. The experimental material on the subject is scanty,^{362,363} and the only donors that have been tested so far are fluorenes. Thus dibiphenyleneethylene (LXXI) adds fluorene under the catalytic influence of sodium hydroxide, to give an 82% yield



LXXI



LXXII

of tribiphenyleneethane (LXXII). The same reaction can be effected between 2,7-dibromofluorene and 2,7,2',7'-tetrabromodibiphenyleneethylene.

It is to be expected that these highly substituted systems will show a considerable tendency to dissociate (in the way that decaphenylbutane dissociates into pentaphenylethyl).³⁶⁴ Thus one can explain the observation that 9-aminofluorene (LXXIII) reacts with dibiphenyleneethylene (LXXIV) in the presence of ammonia to give dibiphenyleneethane (LXXV) and fluorenone imide (LXXVI) by the accompanying equation. 9-Fluorenol behaves analogously. The observation that 2,7,2',7'-tetrabromodibiphenyleneethylene and fluorene yield the dibromo derivative

³⁶⁰ Pullman, Berthier, and Pullman, *Bull. soc. chim. France*, 1950, 1097.

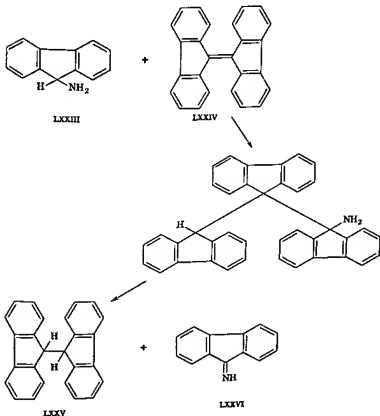
³⁶¹ Bergmann and Fischer, *Bull. soc. chim. France*, 1950, 1084.

³⁶² Pinck and Hilbert, *J. Am. Chem. Soc.*, 68, 2014 (1946).

³⁶³ Pinck and Hilbert, *J. Am. Chem. Soc.*, 68, 2739 (1946).

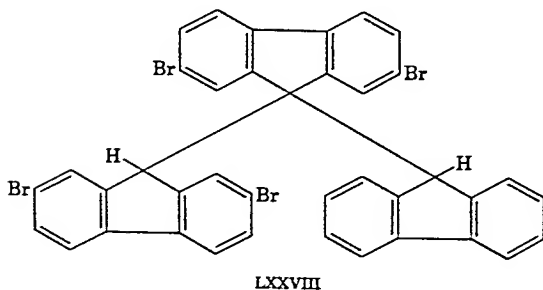
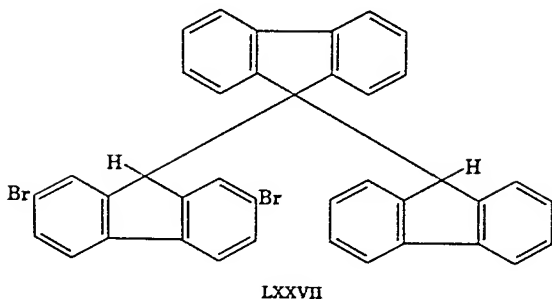
³⁶⁴ Schlenk and Mark, *Ber.*, 55, 2296 (1922).

(LXXVII) and 2,7-dibromofluorene can be understood on the basis of a sequence of condensation and disproportionation steps.

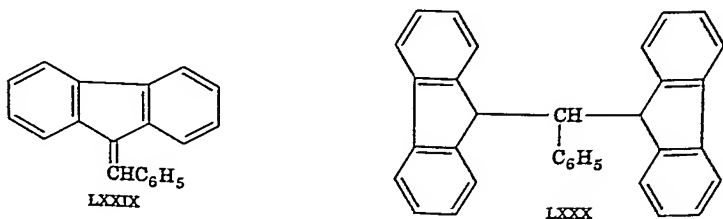


2,7-Dibromofluorene and dibiphenyleneethyne give with sodium ethoxide as catalyst a 58% yield of α -(2,7-dibromobiphenylene)- β , γ -dibiphenylene propane (LXXVII), whereas, in the presence of potassium hydroxide and pyridine, α , β -bis-(2,7-dibromobiphenylene)- γ -biphenylene propane (LXXVIII) is formed. Thermal decomposition of these two propane (LXXVIII) gives, inter alia, 2,7-dibromodibiphenyleneethyne, 2,7-compounds gives, inter alia, 2,7-dibromodibiphenyleneethyne, 2,7-dibromodibiphenyleneethane, 2,7,2',7'-tetrabromodibiphenyleneethyne, and 2,7,2',7'-tetrabromodibiphenyleneethane (formulas on p 244).

The second fulvene derivative that has been employed as an acceptor



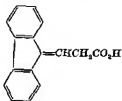
in the Michael condensation is benzylidenefluorene (LXXIX), which adds fluorene in 70% yield under the influence of a mixture of pyridine and aqueous sodium hydroxide. In accordance with the direction of the dipole moment in the semicyclic double bond of the fulvenes, the product is α,γ -dibiphenylene- β -phenylpropane (LXXX).³⁶⁵



It is not surprising that formylfluorene, i.e., 9-hydroxymethylene-fluorene, is also capable of undergoing the Michael condensation (see pp. 221, 235). Formylfluorene has been converted by reaction with malonic

³⁶⁵ Bergmann and Lavie, *J. Am. Chem. Soc.*, **74**, 3173 (1952).

acid (with loss of water and carbon dioxide) to β -(9-fluorenylidene)-propionic acid (LXXXI) in 11% yield.³⁶⁶



LXXXI

Systems That Did Not Undergo Condensation

The following is a list of reactant systems that have not given Michael condensation products. The listing is in order of increasing number of carbon atoms in the acceptor.

Acrylonitrile and diethyl acetosuccinate.³⁶⁷

Methyl vinyl sulfone and ethyl phenylacetate, acetophenone, or benzyl *p*-tolyl sulfone.³¹⁸

Methyl vinyl ketone and "Inhoffen's ketone."³⁶⁸

Methyl isopropenyl ketone and cyclopentanone.³⁶⁹

Acetylacetone and chloroacetamide, phenylacetamide, benzyl cyanide,³⁷⁰ or α -cyanopropionamide.³⁷¹

Ethyl acrylate and 3-acetyloxindole or 1-methyl-3-acetyloxindole.³⁷²

Methyl crotonate and nitropropane in the presence of diethylamine.³⁷³

Mesityl oxide and 2-quinaldine.³⁷⁴

Crotonaldehyde with *N*-(1,3-dimethylbutylidene)-1,3-dimethylbutylamine.³⁷⁵

Ethyl crotonate and 2,7-dibromofluorene.³⁷⁶

p-Benzoquinone and ethyl *N*-acetyl- β -aminocrotonate or diethyl aminomethylenemalonate.³⁷⁷

³⁶⁶ Borsche and Niemann, *Ber.*, 69, 1993 (1936).

³⁶⁷ Blood and Linstead, *J. Chem. Soc.*, 1952, 2256.

³⁶⁸ Pinder and Robinson, *J. Chem. Soc.*, 1952, 1254.

³⁶⁹ Colonge and Dreux, *Bull. soc. chim. France*, 1952, 47.

³⁷⁰ Basu, *J. Indian Chem. Soc.*, 7, 815 (1930) [*C. A.*, 25, 1628 (1931)].

³⁷¹ Bardhan, *J. Chem. Soc.*, 1929, 2223.

³⁷² Julian and Printy, *J. Am. Chem. Soc.*, 75, 5301 (1953).

³⁷³ Klotzel, *J. Am. Chem. Soc.*, 70, 3571 (1948).

³⁷⁴ Weiss and Hauser, *J. Am. Chem. Soc.*, 71, 2026 (1949).

³⁷⁵ Smith, Norton, and Ballard, *J. Am. Chem. Soc.*, 75, 3316 (1953).

³⁷⁶ Taylor and Connor, *J. Org. Chem.*, 6, 695 (1941).

³⁷⁷ Beer, Davenport, and Robertson, *J. Chem. Soc.*, 1953, 1262.

3-Methyl-2-cyclopentenone and ethyl acetoacetate.³⁷⁸

Ethyl α -acetamidoacrylate and oxindole.³⁷⁹

1-Acetylcyclohexene and 6-methoxy-9-methyl-1-keto-1,4,5,6,7,8,9,10-octahydronaphthalene.³⁸⁰

Methyl 5-methyl-2-hexenoate or δ -methylsorbate with dimethyl malonate or methyl cyanoacetate.³⁸¹

1-Acetyl-2-methylcyclohexene with various reagents.³⁸²⁻³⁸⁷

Trimethylquinone and biacetyl or its half-acetal.³⁸⁸

Methyl α -cyano- β -methylsorbate and methyl cyanoacetate.³⁸¹

Ethyl β -diethylaminovinyl ketone and 2-methylcyclohexanone.³⁸⁹

Trimethylquinone monomethylimine and 3,3-dimethoxy-2-butanone.³⁸⁸

Methyl 2-hydroxystyryl ketone and ethyl oxaloacetate, ethyl cyanoacetate, or diethyl malonate.³⁸

Methyl α -cyclohexylideneethyl ketone with diethyl malonate.³⁹⁰

4-Phenyl-2-methylamino-2-buten-4-one and ethyl cyanoacetate.³⁹¹

Diethyl 1-pentene-1,3-dicarboxylate and ethyl cyanoacetate.³⁹²

Ethyl cinnamate or diethyl benzylidenemalonate and fluorene or 2,7-dibromofluorene.³⁷⁶

Diethyl 2-acetyl-2-hexene-1,6-dioate and 1-tetralone or 6-methoxy-1-tetralone.^{206,393}

2-Dimethylamino- or 2-morpholino-benzosuberone or their methiodides with biacetyl or its monoxime.³⁹⁴

3-Phenyl-5,5-dimethyl-2-cyclohexenone and diethyl malonate, ethyl cyanoacetate, or nitromethane.³⁹⁵

3-Benzylidene-6-formylcyclohexanone and 5-diethylaminopentane-2,3-dione-3-monoxime or its methiodide.³⁹⁴

³⁷⁸ Acheson, *J. Chem. Soc.*, 1952, 3415.

³⁷⁹ Julian, Printy, Ketcham, and Doone, *J. Am. Chem. Soc.*, **75**, 5305 (1953).

³⁸⁰ Nazarov and Zav'yalov, *Izvest. Akad. Nauk S.S.S.R. Otdel. Khim. Nauk*, 1952, 437 [*C.A.*, **47**, 5365 (1953)].

³⁸¹ Reid and Sause, *J. Chem. Soc.*, 1954, 516.

³⁸² Bagchi and Banerjee, *J. Indian Chem. Soc.*, **23**, 397 (1946) [*C.A.*, **42**, 1601 (1948)].

³⁸³ Dimroth, *Angew. Chem.*, **59**, 215 (1947).

³⁸⁴ Huber, *Ber.*, **71**, 725 (1938).

³⁸⁵ Johnson, Szmuszkowicz, and Miller, *J. Am. Chem. Soc.*, **72**, 3726 (1950).

³⁸⁶ Ludevitz, Dissertation, Goettingen, 1944.

³⁸⁷ Turner and Voitle, *J. Am. Chem. Soc.*, **72**, 4166 (1950).

³⁸⁸ Smith and Dale, *J. Org. Chem.*, **15**, 832 (1950).

³⁸⁹ Hills and McQuillin, *J. Chem. Soc.*, 1953, 4060.

³⁹⁰ Kon, *J. Chem. Soc.*, 1928, 1792.

³⁹¹ Basu, *J. Indian Chem. Soc.*, **12**, 299 (1935) [*C.A.*, **29**, 6878 (1935)].

³⁹² Thorpe and Wood, *J. Chem. Soc.*, 103, 1579 (1913).

³⁹³ Peak, Robinson, and Walker, *J. Chem. Soc.*, 1938, 752.

³⁹⁴ Tarbell, Wilson, and Ott, *J. Am. Chem. Soc.*, **74**, 6263 (1952).

³⁹⁵ Woods, *J. Am. Chem. Soc.*, **69**, 2549 (1947).

Benzylideneacetophenone and diethyl cyanomalonate,¹²⁵ diethyl ethylmalonate,³⁹⁸ diethyl butylmalonate¹²⁵ or diethyl phenylmalonate¹²⁵

m- or *p*-Nitrobenzylideneacetophenone and fluorene.³⁷⁶

α -Cyanostilbene and ethyl phenylacetate⁶²

Diethyl cinnamylidenemalonate and methyl cyanoacetate³⁹⁷

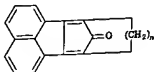
cis-Dibenzoylethylene and diethyl benzylmalonate.⁵⁸

2-Acetyl-1,3-diphenyl-2-propen-1-al and ethyl tetrahydroanthranilate.³⁹⁸

Ethyl 2,4-diphenylbutadiene-1-carboxylate and ethyl cyanoacetate.³⁹⁷

2-(Trimethylquinonyl)methylene-3,5,6-trimethyl-2-acetoxy- (or methoxy)-3,5-cyclohexadienone with diethyl malonate or ethyl cyanoacetate³⁹⁹

Unsaturated carbonyl-bridged system such as



with diethyl malonate or cyanoacetamide.⁴⁰⁰

Diethyl benzylidenemalonate and nitroethane⁸⁶

2,3-Dichloro-1,4-naphthoquinone and acetone.²⁷³

Mesityl oxide and cyclohexanone⁴⁰¹

Acrylonitrile and diethyl trimethylsuccinate, which appears to give an O-substituted derivative of the enol form.⁴⁰²

3-Methyl-4-amino-3-penten-2-one and cyanoacetamide.³⁹⁸

2-Methylcycloheptylideneacetonitrile and cyanoacetamide.^{402a}

Examination of these examples does not lead to definite conclusions as to the factors responsible for the failure of the condensation. However, the qualitative impression gained is that many substituents about the reacting centers tend to prevent the reaction. In the donors, this can be ascribed to lowering acidity, but steric factors undoubtedly also play a part in interfering with the condensation. As a case in point, the failure of diethyl phenylmalonate to undergo any Michael reaction⁴⁰³ may be cited.

³⁹⁸ de Benneville, Clagett, and Connor, *J. Org. Chem.*, **6**, 690 (1941)

³⁹⁹ Bloom and Ingold, *J. Chem. Soc.*, 1931, 2765.

⁴⁰⁰ Basu, *J. Indian Chem. Soc.*, **8**, 319 (1931) [*C.A.*, **26**, 458 (1932)].

⁴⁰¹ Smith, Davis, Jr., and Sogn, *J. Am. Chem. Soc.*, **72**, 3651 (1950)

⁴⁰² Allen and Van Allan, *J. Org. Chem.*, **18**, 882 (1953)

⁴⁰³ Brande and Wheeler, *J. Chem. Soc.*, 1955, 329.

^{402a} Talukdar and Bagchi, *J. Org. Chem.*, **20**, 13 (1955)

^{402b} Kandiah and Linstead, *J. Chem. Soc.*, 1929, 2139.

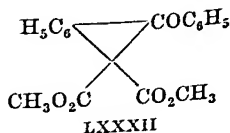
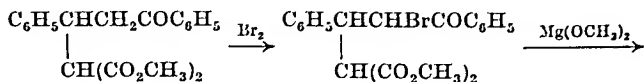
⁴⁰³ Connor, *J. Am. Chem. Soc.*, **55**, 4597 (1933).

SYNTHETIC APPLICATIONS

Certain products of the Michael condensation may be used for the preparation of amino acids; others may undergo spontaneous cyclization or cycloisomerization reactions and thus open routes to a variety of ring compounds. In particular, the Robinson modification of the Michael reaction has been utilized for the synthesis of alicyclic ring systems (Table VIII). It seems, therefore, desirable to give a systematic picture of these synthetic possibilities.

Synthesis of Cyclic Systems

Cyclopropane Rings. Compounds that serve as intermediates for the formation of products containing the cyclopropane ring can be obtained by Michael condensation. For example, the product of the Michael reaction between benzylideneacetophenone and dimethyl malonate can be brominated and dehydrobrominated to yield a cyclopropane



derivative (LXXXII), as shown in the formulation.⁴⁰⁴ Many highly substituted cyclopropane derivatives can be prepared by this route.

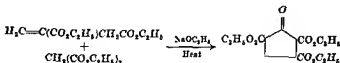
Cyclobutane Rings. It has been reported that cyclobutane derivatives were formed by intramolecular Michael condensation of esters of certain polycarboxylic acids.^{322,323,405} Recent investigations^{324,325} have shown, however, that reaction of diethyl acetylenedicarboxylate with, for example, tetraethyl ethane-1,1,2,2-tetracarboxylate does not give hexaethyl cyclobutane-1,2,3,3,4,4-hexacarboxylate but hexaethyl butene-1,1,2,2,3,4-hexacarboxylate.

Cyclopentane Rings. Cyclopentanone derivatives are formed *in situ* by Dieckmann condensation of the primary adducts of the Michael condensation between ethyl citraconate (or itaconate) and malonates or

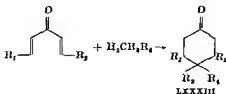
⁴⁰⁴ Kohler and Conant, *J. Am. Chem. Soc.*, **39**, 1404 (1917).

⁴⁰⁵ Guthzeit, Weiss, and Shaefer, *J. prakt. Chem.*, [2], **80**, 393 (1909).

substituted malonates.^{4,145,468} (Compare also the analogous formation of cyclopentanones from cyclopropane derivatives; see pp. 205-207).



Cyclohexane and Condensed Alicyclic Ring Systems. Divinyl ketones of the dibenzylideneacetone type react with donors that contain an active methylene group according to the accompanying general equation, yielding substituted cyclohexanones (LXXXIII)¹⁵⁸⁻²⁰⁹



In general, Michael adducts of unsaturated aldehydes and ketones with ethyl acetoacetate easily undergo a secondary condensation between the terminal methyl group of the adduct and the carbonyl group of the original acceptor molecule. In a fair number of cases, this cyclization reaction is accompanied by the elimination of the carboxy group. This reaction is illustrated by the synthesis of the keto esters LXXXIV,²²⁹ LXXXV,^{15,16,17} and LXXXVI.⁴⁰⁷ In the last example, the reaction stops at the intermediary aldol stage, without the additional dehydration step⁴⁰⁸ (see equations on p. 250).

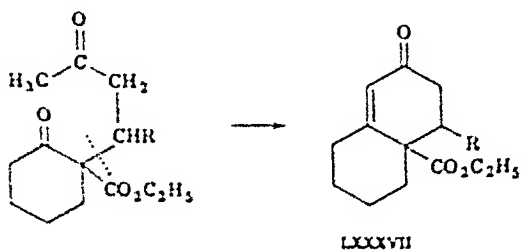
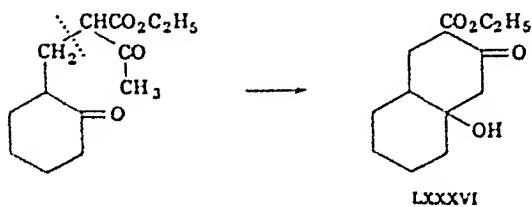
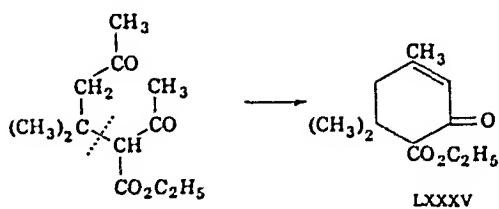
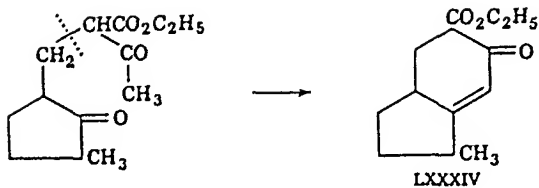
Obviously, the same reaction will take place whenever 1,5-diketones of the above type are formed, e.g., in the condensation product of ethyl cyclohexanone-2-carboxylate and ethylideneacetone or benzylideneacetone, yielding LXXXVII ($\text{R} = \text{CH}_3$ or C_6H_5).⁴⁰⁹ A similar cyclization takes place with the adduct of 1-tetralone and ethylideneacetoacetate or

⁴⁰⁸ Toivonen, John, Sainio, and Kuusinen, *Suomen Kemistilehti*, 5B, 46 (1935) [*C A*, 30, 2185 (1936)].

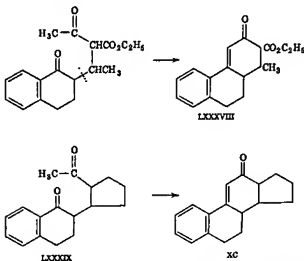
⁴⁰⁷ Mannich, Koch, and Borkowsky, *Ber*, 70, 355 (1937).

⁴⁰⁹ In this and the following formulations, the dotted lines indicate the components from which the starting materials of the cyclization reaction are formed.

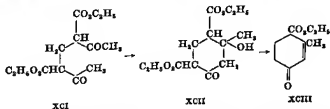
⁴¹⁰ Rapson, *J. Chem. Soc.*, 1936, 1626.



acetylcyclopentene, yielding the tricyclic keto ester LXXXVIII⁴⁰⁶ and (via LXXXIX) the tetracyclic ketone XC,⁴⁰⁷ respectively.



A related reaction is the cyclization of diethyl alkylidenebisacetoacetates. Diethyl methylenebisacetoacetate (XCI), for example, forms XCII: this then loses water and one carboethoxyl group to give the "Hagemann ester" XCIII. In other instances, both carboethoxy groups



are split off and 1-methyl-5-alkyl-1-cyclohexen-3-ones are formed. The reaction of ethyl sodioacetoacetate and ethyl ethoxymethyleneacetoacetate is more complicated.⁴¹⁰⁻⁴¹³ Other examples are the condensation products of mesityl oxide and ethyl benzoylacetate,⁴¹⁴ acetylacetone,⁴¹⁵

⁴⁰⁶ Clausen, *Ann.*, 297, 1 (1897), especially p. 49.

⁴⁰⁷ Liebermann, *Ber.*, 39, 2071 (1906), and previous papers.

⁴⁰⁸ Feist, Delfs, and Langenkamp, *Ber.*, 59, 2958 (1926).

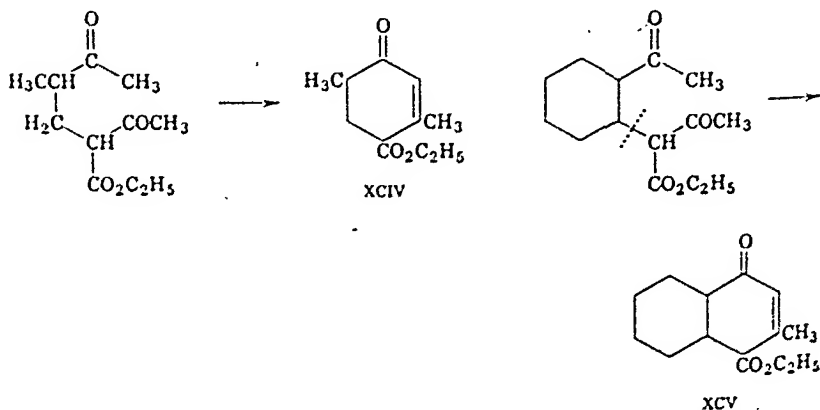
⁴⁰⁹ Feist, Janasen, and Chen, *Ber.*, 60, 199 (1927).

⁴¹⁰ Beringer and Kuntz, *J. Am. Chem. Soc.*, 73, 364 (1951).

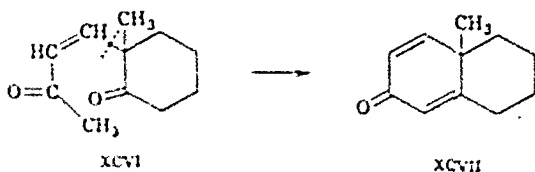
⁴¹¹ Schenber and Meisel, *Ber.*, 48, 236 (1915).

or deoxybenzoin;⁴¹⁶ the 1:2 adducts of diethyl malonate or its mono-substitution products with acrolein and methacrolein;^{410,417} and the condensation products of methyl vinyl ketone with 2-methylcyclopentanone,^{229,230} 2-methylcyclohexanone,²²⁹ or aliphatic ketones.^{418,419}

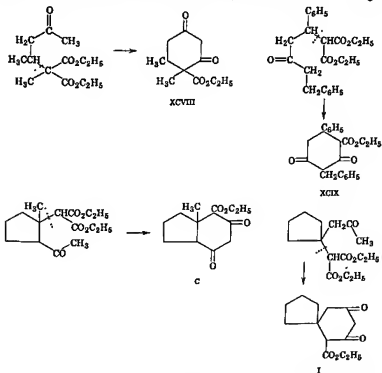
There are a few cases in which the methyl of an acetyl group other than that of the ethyl acetoacetate component supplies the hydrogen for the water molecule to be eliminated, e.g., in the formation of the cyclohexenones XCIV¹²⁰ and XCV.⁹³ This cyclization is also possible with



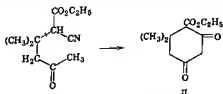
unsaturated 1,5-diketones. Obviously, the configuration of the double bond must be *cis* for cyclization to take place. The product XCVI from acetylacetylene and 2-methylcyclohexanone gives the dienone XCVII.



an ethoxy group and a hydrogen atom in the ϵ position. Cyclic 1,3-diones, such as XCVIII,⁴²² XCIX,⁴²³ C,⁴²⁴ and I,^{424,*} are formed. Analogous



adducts derived from ethyl cyanoacetate (instead of malonate) give the same final products, e g., the cyclohexanedione II⁴²⁵



⁴²² Hinkel, Ayling, Dippy, and Angel, *J. Chem. Soc.*, 1931, 814

⁴²³ Matter, Hastings, and Walker, *J. Chem. Soc.*, 1930, 2455

⁴²⁴ Chuang, Ma, and Tien, *Ber.*, 68, 1846 (1935)

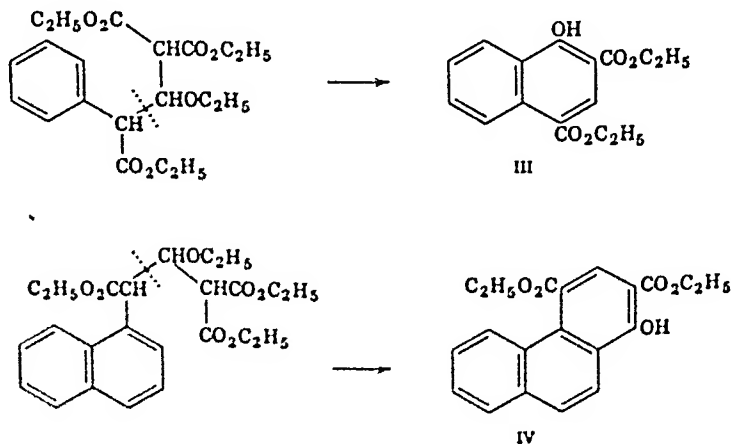
* Enumeration of formulas begins with I again after C to reduce the complexity of the numbers.

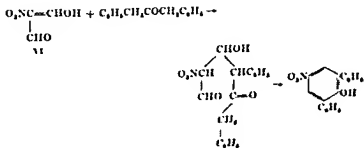
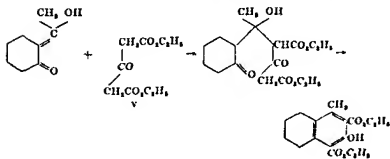
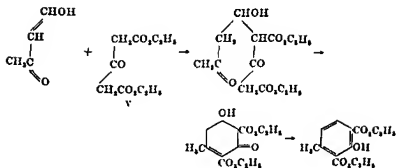
⁴²⁵ Vorländer, *Ann.*, 294, 253 (1897)

Analogous behavior has, of course, been observed with the δ -keto esters formed, for example, from β -keto esters and α,β -ethylenic esters.⁴²⁶

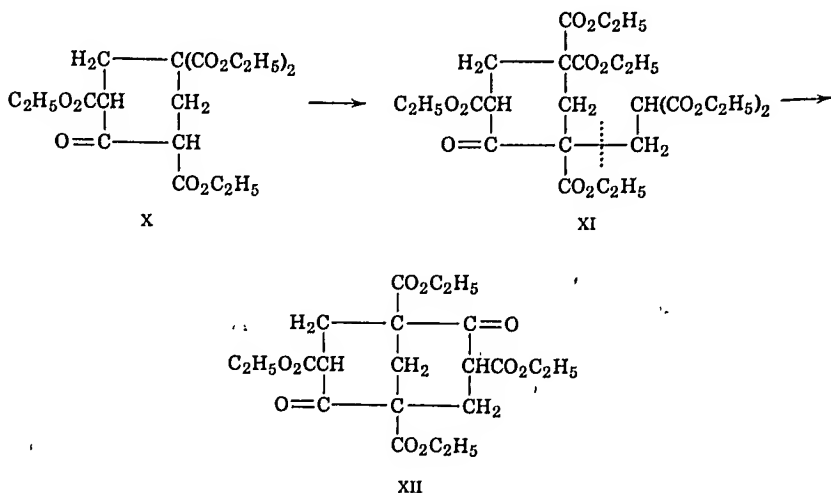
Aromatic Ring Systems. When the δ -keto ester contains a double bond in the β,γ position, the final product is a substituted resorcinol; thus the adduct of diethyl malonate and *n*-butylacetylacetylene gives 5-*n*-butylresorcinol (see p. 214). Other reaction schemes in which aromatic products are formed in the Michael condensation are described in the remaining paragraphs of this section.

Esters of styrylacetic acid, which can be obtained from arylacetates and diethyl ethoxymethylenemalonate, cyclize to derivatives of α -naphthol (III)³⁰³ or hydroxyphenanthrene IV.³⁰⁹ Similarly, the condensation of the enolic forms of β -keto aldehydes and β -diketones with diethyl



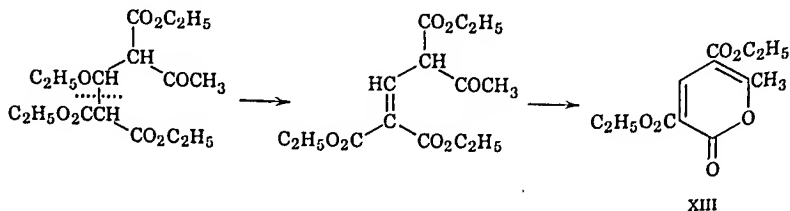


loss of one carbethoxy group beta to the keto group, leads to tetraethyl cyclohexanone-2,4,4,6-tetracarboxylate (X). This can again undergo a Michael reaction with diethyl ethylene-1,1-dicarboxylate to give XI. Renewed Dieckmann reaction and loss of a carbethoxy group yields as



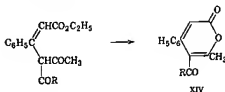
the final product tetraethyl bicyclo[3.3.1]nonane-2,6-dione-1,3,5,7-tetracarboxylate (XII).

Oxygen-Containing Rings. δ -Keto esters containing a double bond in the α,β position cyclize by an entirely different course from their β,γ analogs. Thus, although the β,γ compounds form 5-alkylresorcinols (see p. 214), the adducts of diethyl malonate and hydroxymethylene ketone

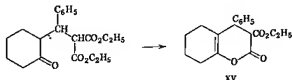


derivatives lose water or ethanol in the course of condensation, and α -pyrone derivatives such as XIII are formed. Another example is the adduct of ethyl acetoacetate and diethyl ethoxymethylene-malonate or -cyanoacetate.³¹⁰ The condensation products of ethyl phenylpropiolate

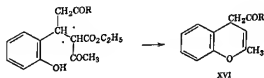
with ethyl acetoacetate^{430,431} and acetylacetone^{432,433} behave analogously, giving XIV ($R = \text{OC}_2\text{H}_5$ and CH_3 , respectively).



An additional case, in which a saturated δ -keto ester is cyclized by enolization of the carbonyl group, is represented by the adduct of cyclohexanone and diethyl benzylidenemalonate. Here, the ε -methylene group is sterically prevented from participation in a potential ring system and the enol lactone XV is formed.



γ -(*o*-Hydroxyphenyl)ketones are converted to 2,3-benzo-1,4 dihydropyran derivatives (XVI, $R = \text{CH}_3$, C_6H_5) under the conditions of the



Michael condensation.^{203,434} Similar ring closures have been treated in an earlier chapter of *Organic Reactions*.⁴³⁵ The adduct from 3-chloro-2-cyclohexen-1-one and diethyl methylmalonate loses hydrogen chloride

⁴³⁰ Feist and Pomme, *Ann.*, **370**, 72 (1909)

⁴³¹ Ruhemann, *J. Chem. Soc.*, **75**, 245 (1899)

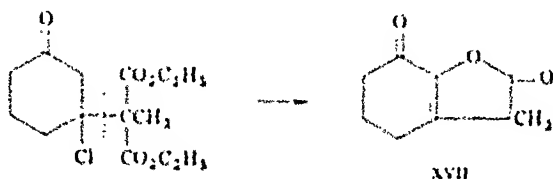
⁴³² Ruhemann, *J. Chem. Soc.*, **75**, 411 (1899)

⁴³³ Ruhemann and Cunningham, *J. Chem. Soc.*, **75**, 778 (1899)

⁴³⁴ Forster and Heilbron, *J. Chem. Soc.*, 125, 340 (1924)

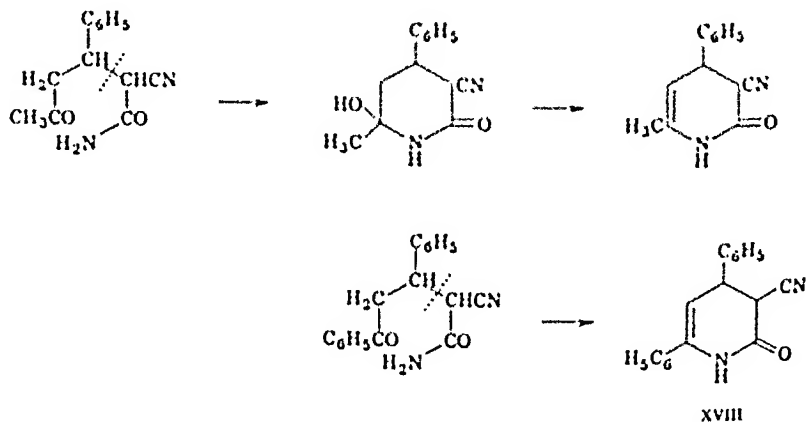
⁴³⁵ Hauser, Swamer, and Adams, in Adams, *Organic Reactions*, Vol. 8, Chapter 3, John Wiley & Sons, 1954. See especially pp. 90-95 and Tables XVI and XVII.

and cyclizes to the saturated lactone XVII.⁴²⁶ Dovey and Robinson⁴²⁷ have suggested that the formation of 2,4,6-triphenylpyrylium fluoroborate



from acetophenone and boron trifluoride takes place by a Michael reaction. However, it has recently been proved that this is not the case.⁴²⁸

Piperidines and Pyridines. δ -Ketonic amides formed by Michael condensations from cyanoacetamide and α,β -ethylenic ketones undergo cyclization to unsaturated cyano-substituted 2-ketopiperidines (XVIII).



The first of the accompanying examples shows a hydroxylated intermediate, such as has been isolated in a number of reactions.⁴²⁹

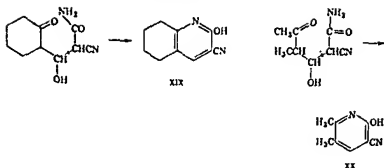
A slightly different scheme applies to the condensation products of cyanoacetamide and α -hydroxymethylene ketones, in which, by the loss of water, a second double bond is introduced into the ring and thus the enolization to 2-hydroxypyridines (XIX and XX) is facilitated.^{171,224} Aminomethylene ketones behave analogously,³⁹⁸ and cyanoacetamide can

⁴²⁶ Paranjpe, Phalnikar, Bhide, and Nargund, *Current Sci. India*, **12**, 150 (1943) [*C.A.*, **37**, 6671 (1943)].

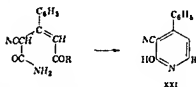
⁴²⁷ Dovey and Robinson, *J. Chem. Soc.*, **1935**, 1389.

⁴²⁸ Elderfield and King, *J. Am. Chem. Soc.*, **76**, 5437 (1954).

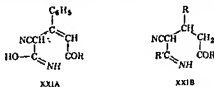
⁴²⁹ Barat, *J. Indian Chem. Soc.*, **7**, 321 (1930) [*C.A.*, **24**, 4786 (1930)].



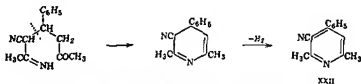
be replaced by malonamide.¹⁷⁹ The same result is obtained with the adducts from cyanoacetamide and acetylenic ketones. Compounds having the general structure XXI ($R = C_2H_5$ or C_6H_5) are formed^{181,184}



If the precursor of XXI is shown in the tautomeric form XXIA, it is evident that compounds of type XXIB will be capable of a similar

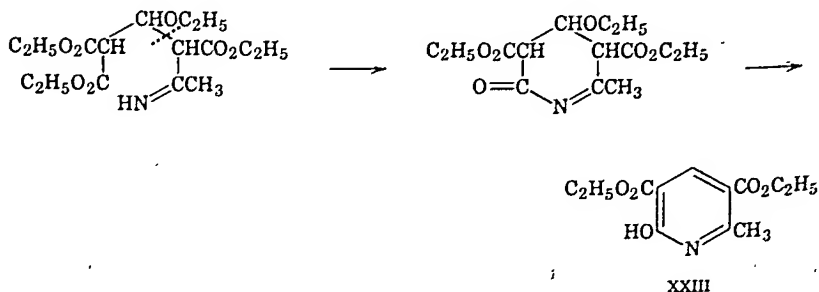


transformation into pyridine derivatives. Thus "diacetonitrile" and benzylideneacetone give, after spontaneous loss of hydrogen from the primary product, 3-cyano-4-phenyl-2,6-dimethylpyridine (XXII).⁴⁴⁰

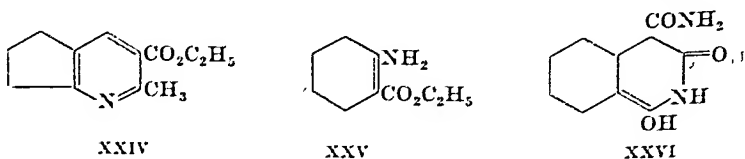


⁴⁴⁰ Chatterjee, *J. Indian Chem. Soc.*, 29, 323 (1952) [*C. A.*, 47, 9972 (1953)].

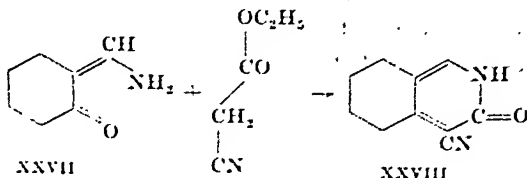
Likewise, the imine of ethyl acetoacetate condenses with diethyl ethoxymethylenemalonate with loss of ethanol to give diethyl 2-hydroxy-6-methylpyridine-3,5-dicarboxylate (XXIII).⁴⁴¹



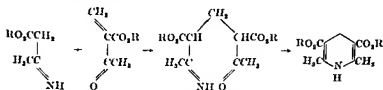
Generally speaking, the imines of β -keto esters and β -diketones react in this manner with hydroxymethylene, alkoxyethylene, and aminomethylene ketones and esters.⁴⁴²⁻⁴⁴⁴ Thus, from 2-hydroxymethylene-cyclopentanone and ethyl iminoacetoacetate, ethyl 5-methyl-4-azaindene-6-carboxylate (XXIV) becomes available.⁴⁴⁵ Also ethyl tetrahydroanthranilate (XXV) reacts in the manner of an aminomethylene ester



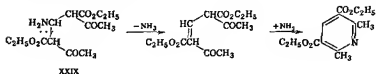
giving with malonamide 1-hydroxy-3-keto-2,3,4,5,6,7,8,10-octahydroisoquinoline-4-carboxamide (XXVI).³⁸¹ The only exception to this rule is the reaction of 2-aminomethylenecyclohexanone (XXVII) with ethyl cyanoacetate, which is claimed⁴⁴⁶ to yield 3-keto-4-cyano-2,3,5,6,7,8-hexahydroisoquinoline (XXVIII). In this connection Berson and



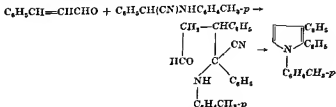
Brown⁴⁴⁷ consider that Hantzsch's synthesis of 1,4-dihydropyridines involves a Michael reaction. These authors assume that, e.g., in the condensation of formaldehyde, ammonia, and ethyl acetoacetate, ethyl β -aminocrotonate and ethyl methyleneacetoacetate are formed and then react in the following way



Another route to the pyridine series is possible in all Michael condensations that lead to 1,5-diketones capable of being cyclized by treatment with ammonia, in these reactions ammonia can be used as the catalyst for the Michael condensation. A special example of this general possibility is provided in the reaction of ethyl aminomethyleneacetoacetate with ethyl acetoacetate or cyclohexanone.⁴⁵⁰ ammonia is eliminated from the primary product XXIX in the first step and utilized in the second step of the subsequent process.



Pyrroles. Clarke and Lapworth⁴⁴⁸ have assumed that the pyrrole synthesis discovered by von Miller and Ploechl⁴⁴⁹ involves a Michael reaction; thus, one could formulate the synthesis of 1-(*p*-tolyl)-2,3-diphenylpyrrole from α -toluidinobenzyl cyanide and cinnamaldehyde in the presence of potassium hydroxide as follows. (Compare ref 450)



⁴⁴⁷ Benson and Brown, *J. Am. Chem. Soc.*, **77**, 444 (1955)

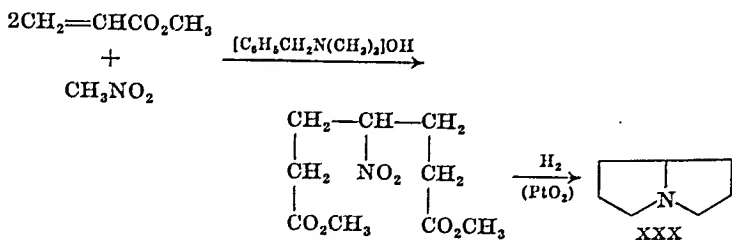
⁴⁴⁸ Clarke and Lapworth, *J. Chem. Soc.*, **91**, 694 (1907)

⁴⁴⁹ Miller and Ploechl, *Ber.*, **31**, 2718 (1898)

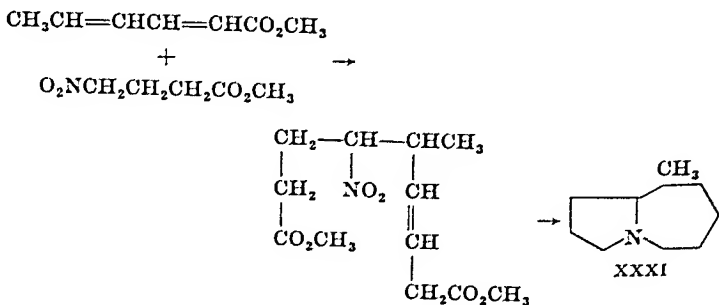
⁴⁵⁰ Bodfors, *Ber.*, **64**, 1111 (1931)

Treibs and Derra,⁴⁵¹ however, have suggested that the synthesis proceeds through a hemiacetal of the unsaturated aldehyde (formed by interaction with the solvent, e.g., methanol) and is, therefore, not a Michael reaction.

Pyrrolizidines and Related Ring Systems. The Michael condensation has been employed by Leonard in the preparation of pyrrolizidines (XXX) by reductive cyclization of γ -nitropimelic esters, which are available from nitroparaffins and acrylates or substituted acrylates.⁴⁵²⁻⁴⁵⁷



Similarly, the reaction has been extended to the synthesis of 6-methylazabicyclo[5.3.0]decane (XXXI) by 1,6-addition of methyl γ -nitrobutyrate to methyl sorbate, followed by reductive cyclization.¹¹⁶



There is also a synthesis of an indole derivative XXXII from quinone and ethyl iminoacetate (β -aminocrotonate),²³⁸ which can be formulated as follows.²³⁸

⁴⁵¹ Treibs and Derra, *Ann.*, 589, 176 (1954).

⁴⁵² Leonard, Hruda, and Long, *J. Am. Chem. Soc.*, 69, 690 (1947).

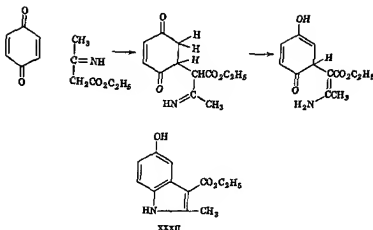
⁴⁵³ Leonard and Beck, *J. Am. Chem. Soc.*, 70, 2504 (1948).

⁴⁵⁴ Leonard and Boyer, *J. Am. Chem. Soc.*, 72, 4818 (1950).

⁴⁵⁵ Leonard and Shoemaker, *J. Am. Chem. Soc.*, 71, 1762 (1949).

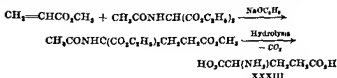
⁴⁵⁶ Leonard and Felley, *J. Am. Chem. Soc.*, 71, 1758 (1949).

⁴⁵⁷ Leonard and Felley, *J. Am. Chem. Soc.*, 72, 2537 (1950).



Synthesis of Amino Acids

The observation that substances such as ethyl acetamidomalonate and ethyl phthalimido-malonate or -cyanoacetate act as donors in the Michael condensation has opened a useful avenue to the synthesis of amino acids.^{461,462-462} The preparation of DL-glutamic acid (XXXIII) illustrates this method.⁴⁶³ The products derived from α,β -ethylenic aldehydes and N-acylated aminomalonates^{460,461,460-462,464} and aminocyanacetates^{460,465} are likewise of considerable interest; they are potential



intermediates in the construction of the ornithine system and appear to be the key substances in the biogenesis of a number of alkaloids.⁴⁴⁵

⁴⁶¹ Albertson and Archer, *J. Am. Chem. Soc.*, **67**, 2043 (1945)

⁴⁶² Galat, *J. Am. Chem. Soc.*, **69**, 963 (1947)

⁴⁶³ Moe and Warner, *J. Am. Chem. Soc.*, **70**, 2763 (1948).

⁴⁶⁴ Rinderknecht and Niemann, *J. Am. Chem. Soc.*, **72**, 2296 (1950)

⁴⁶⁵ Van Zyl, van Tamelen, and Zuidema, *J. Am. Chem. Soc.*, **73**, 1765 (1951).

⁴⁶⁶ Snyder, Shekleton, and Lewis, *J. Am. Chem. Soc.*, **67**, 310 (1945)

⁴⁶⁷ Moe and Warner, *US pat.* 2,508,927 [C.A., **44**, 8274 (1950)]

⁴⁶⁸ Robinson, *Proc. Univ. Durham Phil. Soc.*, **8**, Pt. 1, 14 (1927-1928) [C.A., **23**, 1683 (1929)]

As esters of nitroacetic acid become more generally available, these may also be used in the synthesis of amino acid precursors through the Michael condensation.^{105,466}

EXPERIMENTAL CONDITIONS

Solvents. If the products are sensitive to alcoholysis or if there is competition between the alkoxide ion and the donor anion for the acceptor molecule, a non-hydroxylic solvent is chosen or the reaction is carried out without solvent. Compare, however, ref. 278. When such competition is encountered or when the enolate of the donor is prepared with difficulty, sodium or sodium amide in an inert solvent may be used. Solvents used most often in the Michael condensation are methanol, ethanol, *t*-butyl alcohol, ether, benzene, dioxane, and mixtures of these solvents. Ester exchange has been observed in some condensations in which esters were employed as reactants.¹⁶³

Catalysts. The following catalysts have been used: sodium methoxide, sodium ethoxide, potassium methoxide, potassium ethoxide, potassium isopropoxide, potassium *n*-butoxide, potassium *t*-butoxide, potassium α,α -dimethylpropoxide; dry or aqueous sodium or potassium hydroxide, methanolic or ethanolic sodium or potassium hydroxide, potassium hydroxide in *t*-butanol; metallic sodium or potassium; ammonia, alcoholic ammonia, ammonia in conjunction with ammonium chloride, sodium amide as such or in liquid ammonia; diethylamine, diisopropylamine, piperidine, pyridine, triethylamine, tributylamine, and other trialkylamines; methyltriethylammonium hydroxide, benzyltrimethylammonium hydroxide (Triton B), and its methoxide or butoxide.

Calcium and sodium hydride have been used very rarely;^{166,466a,467} the same applies to potassium carbonate²⁰⁶ and sodium triphenylmethide,⁴⁶³ which was used as condensing agent for Michael reactions with the ethyl esters of acetic, isobutyric, and phenylacetic acids. The first ester underwent Claisen condensation under these conditions before Michael reaction took place.

Aqueous sodium cyanide was employed as catalyst in the condensations of acrylonitrile with ethyl cyanoacetate or benzyl cyanide.⁴⁶²

It is worthy of note that the reaction between cyclohexanone or 2-methylcyclohexanone and acrylonitrile, carried out in the presence of

⁴⁶⁶ E. D. Bergmann, unpublished results.

^{466a} Fishman and Zuffanti, *J. Am. Chem. Soc.*, **73**, 4466 (1951).

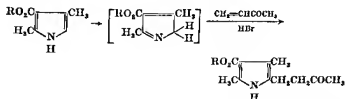
⁴⁶⁷ McElvain and Lyle, Jr., *J. Am. Chem. Soc.*, **72**, 384 (1950).

⁴⁶³ Hauser and Abramovitch, *J. Am. Chem. Soc.*, **82**, 1763 (1960).

¹⁶⁶ Rogers, U.S. pat. 2,460,536 [*C.A.*, **43**, 3446 (1949)].

optically active quartz, coated with sodium, potassium, or lithium ethoxide, has been reported to give slightly optically active products.⁴⁷⁰

Several examples have been reported^{155,255,471-473} of Michael-type condensations brought about by acidic catalysts such as boron trifluoride, zinc chloride, or sulfur dioxide. Of practical importance are the condensations of pyrrole derivatives with free α positions which react with α,β -unsaturated aldehydes, ketones, acids, and acid derivatives in the presence of acidic catalysts such as boron trifluoride etherate or hydrobromic acid^{474,475}. As in the case of indole (see p. 209), one can assume that the donor is a tautomeric form of the pyrrole, in which the α position is transformed into an (activated) methylene group. This product reacts further to give a dipyrrolyltrimethine derivative.



One or two condensations have been effected without an added catalyst. Thus condensation occurs when ethyl hydroxymethylenephénylacetate is heated with malonic or cyanoacetic acid,^{366,476,477} and when methyl vinyl ketone vapor is passed together with acetone or methyl ethyl ketone through a hot tube.⁴¹⁹

Particular mention should be made of the possibility offered by the recent development of strongly basic exchange resins; they appear to be highly promising condensing agents, especially where either a reactant or a reaction product is sensitive to dissolved alkali. Thus acetone or methyl ethyl ketone reacts easily with acrylonitrile in the presence of quaternized cross-linked polyvinylpyridine resin.⁴⁷⁸ More complicated reactions can also be catalyzed in this way.^{479,480}

⁴⁷⁰ Terent'ev, Klabunovskii, and Budovskii, *Sbornik Statei Obshchei Khim.*, **2**, 1612 (1933) [*C.A.*, **49**, 5263 (1955)].

⁴⁷¹ Hauser, *J. Am. Chem. Soc.*, **60**, 1937 (1938).

⁴⁷² Hauser and Breslow, *J. Am. Chem. Soc.*, **62**, 2389 (1940).

⁴⁷³ Berlin and Sherlin, *J. Gen. Chem. USSR*, **8**, 16 (1938) [*C.A.*, **32**, 6397 (1938)].

⁴⁷⁴ Treibe and Muehl, *Ann.*, **589**, 163 (1954).

⁴⁷⁵ Treibe and Herrmann, *Ann.*, **592**, 1 (1955).

⁴⁷⁶ Phalnikar and Nargund, *J. Univ. Bombay*, **4**, 106 (1935) [*C.A.*, **30**, 5106 (1936)].

⁴⁷⁷ Phalnikar and Nargund, *J. Am. Chem. Soc.*, **61**, 1242 (1939).

⁴⁷⁸ Harris, Stiller, and Folkers, *U.S. pat.* 2,579,590 [*C.A.*, **46**, 7114 (1952)].

⁴⁷⁹ E. D. Bergmann and R. Korvitt, *J. Org. Chem.*, **21**, 107 (1956). **23**, 1507 (1958).

⁴⁸⁰ Schmiele and Mansfield, *U.S. pat.* 2,658,070 [*C.A.*, **48**, 13715 (1954)].

EXPERIMENTAL PROCEDURES

γ -Acetamido- γ -carbethoxy- γ -cyanobutyraldehyde.⁴⁴⁸ A solution of 50 mg. of sodium in 60 ml. of absolute ethanol is mixed with 17 g. of ethyl acetamidocyanoacetate, and the resulting suspension is cooled in a water bath while 7.5 ml. of acrolein is added dropwise. After the addition is complete, the mixture is stirred for two hours and neutralized with glacial acetic acid. The mixture is filtered, and the filtrate, after refrigeration for twenty-four hours, deposits the crystalline product. Filtration yields 15 g. (66%) of material melting at 106–109°. Crystallization from 95% ethanol raises the melting point to 113.5–114.5°.

5-Nitro-4,4-dimethylpentan-2-one.³⁰⁹ A mixture of 1 mole of mesityl oxide, 10 moles of nitromethane, and 1 mole of diethylamine is allowed to stand at 30° for thirty days. Unreacted material is removed by distillation up to 55°/20 mm., and the residue is fractionated. After a forerun of 4-diethylamino-4-methylpentan-2-one (10%), the product distills as an oil, b.p. 112–113.5°/14 mm. (65%). The product may be completely freed of basic impurities by shaking with 10% hydrochloric acid. After two distillations, a pure product, boiling at 128–129°/22 mm., can be obtained in 58% yield.

The same product may be obtained in 55–60% yield by heating the reaction mixture under reflux for forty-eight hours and treating subsequently as above.

7-Keto-1-methoxy-13-methyl-5,6,7,9,10,13-hexahydrophenanthrene (Robinson's modification).³¹⁸ While 15.05 g. of diethylaminobutanone⁴⁴⁹ is swirled gently in a 1-l. flask and cooled in ice, 15.0 g. of methyl iodide is added portionwise during thirty minutes. The swirling is regulated so as to obtain the crystalline methiodide as an even coating on the walls of the flask. When no more liquid remains, the flask is kept in ice for thirty minutes and then under the tap for forty-five minutes. A solution of 20.0 g. of 5-methoxy-1-methyl-2-tetralone in 100 ml. of dry thiophene-free benzene is added, air is expelled by dry nitrogen, and a solution of 6.5 g. of potassium in 100 ml. of dry ethanol is added with cooling during five minutes.

Swirling is continued until the methiodide dissolves (about thirty minutes) and is replaced by a precipitate of potassium iodide. The mixture is kept in ice for an additional hour, and then boiled gently for twenty-five minutes. An excess of 2 *N* sulfuric acid is added, followed by enough water to dissolve the potassium sulfate. The benzene layer is separated and the aqueous layer extracted twice with ether. The ether and benzene layers are combined, washed with water, and clarified with

⁴⁴⁸ Wilds and Shunk, *J. Am. Chem. Soc.*, 65, 469 (1943).

magnesium sulfate, and the solvents are evaporated. The residue is distilled and 23.2 g. of product is collected up to 180°/0.1 mm. Crystallization from ether yields 17 g. of product, m.p. 115–117°. An additional gram of material is obtained by distillation of the mother liquors, making a total yield of 18 g. (71%).

This procedure is a general one, in which sodium methoxide or sodium ethoxide may be used effectively as a catalyst.

trans-3-Keto-2-phenylcyclohexanecetic Acid.¹⁰⁸ A mixture of 50 g. of 2-phenyl-2-cyclohexen-1-one, 150 g. of dibenzyl malonate, and a solution of potassium *t*-butoxide, prepared from 1.3 g. of potassium and 20 ml. of *t*-butyl alcohol, is kept at 60° for three hours, and then left overnight at room temperature. The mixture is acidified with 2.5 ml. of acetic acid and diluted to a volume of 250 ml. with ethyl acetate. Thirteen grams of 10% palladium-charcoal is added, and the mixture is hydrogenated for an hour at room temperature at an initial pressure of 4 atm. The catalyst is filtered, the solvent evaporated, and the residue is heated for 10 minutes at 170–180° to effect decarboxylation of the malonic acid. The residue is taken up in ether, the solution extracted several times with 10% sodium carbonate solution, and the alkaline extract acidified. The product is obtained as a solid, m.p. 125° (55 g., 82%).

Dibenzyl malonate is preferred to diethyl malonate as a donor if further hydrolysis of the Michael condensation adduct is desired.

Methyl 3-Keto-2-phenylcyclohexyl- α -nitroacetate.^{106,108} A mixture of 17.2 g. of 2-phenyl-2-cyclohexen-1-one, 23.0 g. of methyl nitroacetate,⁴⁸⁶ and 0.025 mole of 30% methanolic solution of benzyltrimethylammonium methoxide⁴⁸⁷ is allowed to stand at 60° for twelve hours. The mixture is acidified with acetic acid and extracted with ether, and the extract is washed with water and with sodium bicarbonate solution to remove most of the unchanged ester. After removal of the rest of the unreacted materials by distillation in high vacuum, 26.2 g. of product (90% yield) is obtained as an oil.

Triethyl α -Acetyltricarballylate.⁴⁸³ To 20 g. of technical potassium hydroxide in 150 ml. of acetaldehyde dipropyl acetal are added 51.6 g. of diethyl maleate and 52 g. of ethyl acetoacetate, the temperature being maintained at 20° during the addition. The temperature then rises spontaneously to 27°, and the mixture is heated at 90° for one hour. After acidification with dilute sulfuric acid, the acetal layer is separated, the solvent is removed, and the residue distilled in vacuum. Some ethyl acetoacetate is recovered, and 65 g. of product is obtained as an oil,

¹⁰⁸ Feuer, Hass, and Warren, *J. Am. Chem. Soc.*, **71**, 3078 (1949).

¹⁰⁶ Croxall and Schneider, *J. Am. Chem. Soc.*, **71**, 1257 (1949). Cf. Meisenheimer, *Ann.*, **397**, 295 (1913).

b.p. 189°/12 mm. The yield based on material that entered the reaction is 72%.

Diethyl 6-Keto-4-methyl-2-heptene-1,5-dicarboxylate.⁴⁴⁴ To a solution of 2.5 g. of potassium in 150 ml. of absolute *t*-butyl alcohol are added 98 g. of ethyl acetoacetate and 53 g. of ethyl sorbate. The mixture is heated under reflux in an oil bath at 110–120° for twelve hours. The cooled solution is poured into dilute sulfuric acid and the precipitated oil taken up in benzene. After removal of the benzene and unreacted material by distillation, 78 g. of product (75% yield) is obtained as an almost colorless oil, b.p. 120°/0.5 mm.

Hexaethyl 3-Butene-1,1,2,2,3,4-hexacarboxylate.^{321,322,445} Under anhydrous conditions and with stirring, a mixture of 34 g. of diethyl acetylenedicarboxylate, 66 g. of tetraethyl ethane-1,1,2,2-tetracarboxylate, and 10 ml. of absolute ethanol is heated to 45° to obtain a clear solution. A solution of 1.5 g. of sodium dissolved in 24 ml. of absolute ethanol is added dropwise with rapid stirring. After addition of about 10 drops of ethoxide solution, the temperature of the reaction mixture suddenly rises to 92° and then slowly falls as the rest of the catalyst is added. As the temperature rises, the color of the solution changes to dark brown. The mixture is poured into 100 ml. of *N* hydrochloric acid and is exhaustively extracted with ether. Evaporation of the ether leaves a mixture of solid and oil. The solid is collected and crystallized from 80% ethanol. The product, obtained in several crops, weighs 48.5 g. (48%) and melts at 78°.

Diethyl α,β -Diphenylglutarate.^{31,32} One hundred grams of ethyl cinnamate and 100 g. of ethyl phenylacetate are mixed with a solution of 4 g. of sodium in 60 ml. of ethanol and heated under reflux for two and one-half hours. The mixture is neutralized with the calculated amount of dilute hydrochloric acid, and enough water is added to produce turbidity. When the solution is cooled, the product crystallizes in quantitative yield as a mixture of isomers. After several crystallizations from dilute ethanol, the product melts at 92–93°.

Ethyl α -Benzoyl- γ -(2-pyridyl)butyrate.⁴⁹⁰ To a mixture of 246 g. of freshly distilled ethyl benzoylacetate and 66 g. of freshly distilled 2-vinylpyridine, 1 g. of sodium is added, and the mixture is boiled for five hours. The solution is cooled, acidified, and extracted with ether to remove neutral material. The aqueous layer is made alkaline, the oil that separates is taken up in ether, and the extract is dried over anhydrous calcium sulfate. The ether and 2-vinylpyridine are evaporated under reduced pressure, and the residue is distilled to furnish 135 g. (70%) of the product as a pale orange oil, b.p. 170–175°/0.3 mm.

TABULAR SURVEY OF THE MICHAEL CONDENSATIONS

The following tables summarize the data in the literature through October 1955. Tables I–XXI classify the material according to the unsaturated acceptors. Table XXII lists most of the important donors that have been used in the Michael condensation.

The acceptors in Tables I–XXI have been arranged according to increasing number of carbon atoms unless otherwise stated. Alkyl esters are listed (independent of the number of the carbon atoms in the alkyl group) under the lowest member of the series employed. With each acceptor, the donors have been listed according to the following scheme:

Esters and other acid derivatives (except nitriles)

Keto esters

Cyano compounds

Aldehydes and ketones

Nitro compounds

Sulfones


Miscellaneous donors

Commas between items in the catalyst column separate the components of a catalyst combination; semicolons are used to separate different catalyst combinations.

When yields are cited, the first references cited are those to the articles containing the information on yields.

⁴⁹⁰ Bockelheide and Agnello, *J. Am. Chem. Soc.*, **72**, 5005 (1950).

TABLE I
MICHAEL CONDENSATIONS WITH α,β -ETHYLENIC ALDEHYDES

Reactants	Catalyst	Product (Yield, %)	References
Acrolein and Diethyl malonate	NaOC_2H_5 $(n\text{-C}_4\text{H}_9)_3\text{N}$ NaOC_2H_5 NaOC_2H_5 NaOC_2H_5 NaOC_2H_5 NaOC_2H_5 $(n\text{-C}_4\text{H}_9)_3\text{N}; \text{NaOC}_2\text{H}_5$ $(n\text{-C}_4\text{H}_9)_3\text{N}$ NaOC_2H_5 Na	$\text{ACH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (50) $\text{A}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)_4$ $\text{AC}(\text{C}_2\text{H}_5)(\text{CO}_2\text{C}_2\text{H}_5)_2$ (40) $\text{AC}(\text{C}_4\text{H}_9)_2(\text{CO}_2\text{C}_2\text{H}_5)_2$ $\text{AC}(\text{C}_{10}\text{H}_{21})_2(\text{CO}_2\text{C}_2\text{H}_5)_2$ $\text{AC}(\text{C}_{18}\text{H}_{35})_2(\text{CO}_2\text{C}_2\text{H}_5)_2$ $\text{ACBr}(\text{CO}_2\text{C}_2\text{H}_5)_2$ $\text{ACCl}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (76) $\text{AC}(\text{NHCHO})(\text{CO}_2\text{C}_2\text{H}_5)_2$ $\text{AC}(\text{NHCOCH}_3)(\text{CO}_2\text{C}_2\text{H}_5)_2$ (87) $\text{AC}(\text{NHCOCH}_3)(\text{CO}_2\text{C}_2\text{H}_5)_2$ (61) $\text{AC}(\text{NHCOCH}_3)(\text{CO}_2\text{C}_2\text{H}_5)_2$ (56) $\text{AC}(\text{NHCOCH}_3)(\text{CO}_2\text{C}_2\text{H}_5)_2$ (52)†	159, 417, 491 402 159, 161, 491 159, 161, 491 159, 161, 491 491 159, 493 493 494 460 481 462, 494, 495 496
Diethyl phthalimidomalonate	NaOC_2H_5		460, 494

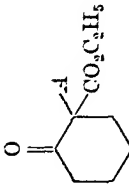
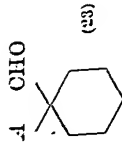
Note: References 491-1045 are on pp. 545-555.


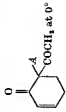

* When sodium ethoxide was used as the catalyst, dehydrohalogenation took place.

† The product was isolated as the phenylhydrazone.

TABLE I—Continued

MICHAEL CONDENSATIONS WITH α,β -ETHYLENIC ALDEHYDES

Reactants	Catalyst	Product (Yield, %)	References
<i>Acrolein (Cont.) and</i>		$A = -CH_2CH_2CHO$	
Diethyl acetoxymalonate	$NaOC_2H_5$	$CH_3CO_2C(A)(CO_2C_2H_5)_2$	159, 497
$CH(CO_2C_2H_5)_2$	$NaOC_2H_5$	$A_2C(CO_2C_2H_5)_2$; 5,5-dicarbethoxy-1-cyclohexene-1-carboxaldehyde	110, 417
CH_3CH_2CHO			
Ethyl acetate	$NaOC_2H_5$	$CH_3COCH(A)CO_2C_2H_5$ (40, 39); 2-cyclohexen-1-one (20, 23)	498, 499
	$NaOC_2H_5$	$CH_3COCH(A)CO_2C_2H_5$	500
	Not indicated	2-Cyclohexen-1-one	501
Ethyl methylacetate	$NaOC_2H_5$	6-Methyl-2-cyclohexen-1-one (20)	499
			162
Ethyl cyclohexanone-2-carboxylate	$NaOC_2H_5$	$ACH(CN)CO_2C_2H_5$ (12); 5-carbethoxy-5-cyano-1-cyclohexene-1-carboxaldehyde	159, 417, 502, 503
Ethyl cyanacetate	$NaOC_2H_5$	$AC(NHCOCH_3)(CN)CO_2C_2H_5$ (82, 80)	460, 494, 504
Ethyl acetamidocyanacetate	$NaOC_2H_5$	$A_2C(CN)CO_2C_2H_5$ (18)	110, 417
$CH(CN)CO_2C_2H_5$			
CH_3CH_2CHO			
Cyclohexanecarboxaldehyde	SO_2	 (23)	472

3-Cyclohexene-1-carboxaldehyde	SO ₂	 (27)	472
Deoxybenzoin	NaOC ₂ H ₅	C ₆ H ₅ CH(A)COC ₆ H ₅ (100)	163
Acetylacetone	Pyridine	CH ₃ COCH(A)COCH ₃ (27); 6-Acetyl-2-cyclohexen-1-one (13); compound C ₁₂ H ₁₄ O ₄ (27);	505
		 at 0°	
Nitromethane	[C ₆ H ₅ CH ₂ N(CH ₃) ₂]OH; NaOCH ₃	ACH ₃ NO ₂ (41)	506
Nitroethane	[C ₆ H ₅ CH ₂ N(CH ₃) ₂]OH; NaOCH ₃	CH ₃ CH(A)NO ₂ (51)	506
1-Nitropropane	NaOC ₂ H ₅	CH ₃ CH ₂ CH(A)NO ₂ (30)	507
2-Nitropropane	[C ₆ H ₅ CH ₂ N(CH ₃) ₂]OH; NaOCH ₃	(CH ₃) ₂ C(A)NO ₂ (49)	506
	NaOC ₂ H ₅	(CH ₃) ₂ C(A)NO ₂ (33)	506
	K ₂ CO ₃	(CH ₃) ₂ C(A)NO ₂	507
Ethyl nitroacetate	NaOC ₂ H ₅	(CH ₃) ₂ C(A)NO ₂ (35)	508
Diethyl nitromalonate	NaOC ₂ H ₅	ACH(NO ₂)CO ₂ C ₂ H ₅	509
	Exchange resin (HO- or CN--form)	AC(NO ₂)CO ₂ C ₂ H ₅ _{1/2}	510
		AC(NO ₂)CO ₂ C ₂ H ₅ _{1/2} (94)	496
(CH ₃) ₃ CHCH ₂ C(CH ₃)=	None	NCH(CH ₃)CH ₂ CH(CH ₃) ₂	
NCH(CH ₃)CH ₂ CH(CH ₃) ₂		 (5)	375

Note: References 491-1045 are on pp. 545-555.

TABLE I—Continued

MICHAEL CONDENSATIONS WITH α,β -ETHYLENIC ALDEHYDES			
Reactants	Catalyst	Product (Yield, %)	References
β -Hydroxycrotonaldehyde and $\text{H}_2\text{NC}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5\parallel$	None	Ethyl 2-amino-6-methylpyridine-3-carboxylate (13)	514
β,β -Dimethylacrolein and β,β -Dimethylacrolein	NaNH_2	4,6,6-Trimethyl-1,3-cyclohexadiene-4-carboxaldehyde	516
β -Ethoxyacrolein \parallel and $\text{H}_2\text{NC}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5\parallel$ $\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CN}$ $\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{COCH}_3$ $\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{COC}_6\text{H}_5$	None None None None None	Ethyl 2-aminopyridine-3-carboxylate (18) Ethyl 2-methylpyridine-3-carboxylate (30) 3-Cyano-2-methylpyridine (4) 3-Acetyl-2-methylpyridine (25) 3-Benzoyl-2-methylpyridine (5)	514 515 515 515 515
β -Ethoxycrotonaldehyde \parallel and $\text{H}_2\text{NC}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5\parallel$ $\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CN}$ $\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{COCH}_3$ $\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{COC}_6\text{H}_5$	None None None None None	Ethyl 2-amino-6-methylpyridine-3-carboxylate Ethyl 2,6-dimethylpyridine-3-carboxylate (40) 3-Cyano-2,6-dimethylpyridine (40) 3-Acetyl-2,6-dimethylpyridine (40) 3-Benzoyl-2,6-dimethylpyridine (35)	514 166 166 166 166
α -Methyl- β -ethylacrolein and Isobutyraldehyde	KOCH_3 , aq. NaOH , 130–180°	$\text{CH}_3\text{CH}_2\text{CHCH}(\text{CH}_3)\text{C}\equiv\text{O}$ (42, 15) $(\text{CH}_3)_2\text{C}=\text{CH}_2-\text{O}$ $\text{CH}_3\text{CH}_2\text{CHCH}(\text{CH}_3)\text{CHO}$ $\text{C}_6\text{H}_5\text{CHCOC}_6\text{H}_5$	165, 164 . 163
Deoxybenzoin	NaOCH_3		

<i>α</i> -Ethyl-β <i>n</i> -propylacrolein and Ethyl acetoacetate	KOH, acetal	$n\text{-C}_2\text{H}_5\text{CHCH}(\text{C}_2\text{H}_5)\text{CHO}$ (31)	483, 517, 518
Butyraldehyde**	Aq NaOH, 200°	$\begin{array}{c} \text{CH}_3\text{COCHCO}_2\text{C}_2\text{H}_5 \\ \\ n\text{-C}_2\text{H}_5\text{CHCH}(\text{C}_2\text{H}_5)\text{C}=\text{O} \\ \\ \text{C}_2\text{H}_5\text{CH}-\text{CH}_2-\text{O} \end{array}$	164
Cinnamaldehyde and Diethyl ethylmalonate Diethyl acetamidomalonalate Ethyl acetoacetate Ethyl <i>n</i> -butylcyanoacetate Ethyl formamidoacyanoacetate Phenylacetaldehyde Deoxybenzoin 1-Nitropropane 2-Nitropropane	$\begin{array}{c} \text{NaOCH}_3 \\ \text{NaOC}_2\text{H}_5 \\ \text{NaOC}_2\text{H}_5 \\ \text{NaOCH}_3 \\ \text{NaOC}_2\text{H}_5 \\ \text{NaOCH}_3 \\ \text{NaOCH}_3 \\ \text{NaOC}_2\text{H}_5 \\ \text{NaOC}_2\text{H}_5 \\ \text{NaOC}_2\text{H}_5 \end{array}$	$\begin{array}{c} A = \text{C}_6\text{H}_5\text{CHCH}_2\text{CHO} \\ \text{AC}(\text{C}_2\text{H}_5)(\text{CO}_2\text{C}_2\text{H}_5)_2 \\ \text{AC}(\text{NHCOCH}_3)(\text{CO}_2\text{C}_2\text{H}_5)_2 \\ \text{6-Carbethoxy-5-phenyl-2-cyclohexen-1-one} \\ \text{AC}(\text{C}_2\text{H}_5)_n(\text{CN})(\text{CO}_2\text{C}_2\text{H}_5) \\ \text{AC}(\text{NHCHO})(\text{CN})(\text{CO}_2\text{C}_2\text{H}_5) \\ \beta,\gamma\text{-Diphenylvalerolactone (18)} \\ \text{C}_6\text{H}_5\text{CH}(A)\text{COC}_6\text{H}_5 \text{ (quant.)} \\ \text{CH}_3\text{CH}_2\text{CH}(A)\text{NO}_2 \\ (\text{CH}_3)_2\text{C}(A)\text{NO}_2 \end{array}$	519 464 512 519 464 163 163 520 520
β-Hydroxycinnamaldehyde and $\text{H}_2\text{NC}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	None	Ethyl 2-amino 6-phenylpyridine-3-carboxylate (31)	521
2-Heptylidenheptanal†† and Heptanal	Aq. NaOH, 200°	3 <i>n</i> -Hexyl-2,4-di- <i>n</i> pentylvalerolactone (9)	167

Note: References 491-1045 are on pp. 545-555.

|| Malonic acid ethyl ester imino ether was employed; it reacted as the amidine.

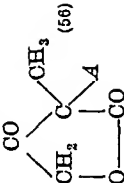
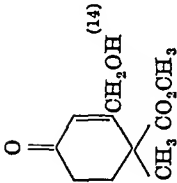
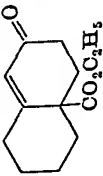
† The aldehyde was introduced in the form of its acetal.


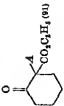
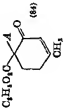


** The butyraldehyde was formed *in situ* by scission of α -ethyl-β-*n*-propylacrolein.

†† The unsaturated aldehyde was formed *in situ* from heptanal.

TABLE II

MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC KETONES

Reactants	Catalyst	Product (Yield, %)	References
<i>Methyl Vinyl Ketone and</i> Diethyl malonate Diethyl ethylmalonate	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{OH})_2]_2\text{OH}$ NaOC_2H_5	$A = \text{CH}_3\text{COCH}_2\text{CH}_2-$ $A_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (85) $\text{AC}(\text{C}_2\text{H}_5)(\text{CO}_2\text{C}_2\text{H}_5)_2$ (42)	522, cf. 523 524
α -Methyl- β -oxo- γ -butyrolactone	NaOCH_3	 (56)	525
	NaOCH_3^*	 (14)	525
Ethyl acetoacetate Ethyl ethylacetoacetate Ethyl α -(methylthiomethyl)- acetoacetate Ethyl isopropylacetoacetate†	NaOC_2H_5 Na NaOC_2H_5 NaOC_2H_5	$\text{CH}_3\text{COC}(\text{A})_2\text{CO}_2\text{C}_2\text{H}_5$ (92) 4-Ethyl-3-methyl-2-cyclohexen-1-one $\text{CH}_3\text{COC}(\text{CH}_2\text{SCH}_3)(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (47)	119 420 526
	NaOC_2H_5	6-Carboxy- β -isopropyl-3-methyl-2-cyclohexen- 1-one (32)††† $\text{CH}_3\text{COC}(\text{A})(\text{C}_3\text{H}_7)\text{CO}_2\text{C}_2\text{H}_5$ (74)	527 119
Ethyl 2-oxocyclohexane-1- carboxylate†	NaOH	 (small)	528

Not indicated		529
Ethyl 4-methyl-2-oxo-3-cyclohexene-1-carboxylate	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$ 	530
NaOCH_3		122
Ethyl benzoylacetate	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$ 	538
Ethyl (α-furoyl)acetate	Not indicated 	531

4-Carboethoxy-3-(α-furyl)-3-hydroxycyclohexan-1-one

Note: References 491-1045 are on pp. 545-555.

* In this condensation the amount of catalyst was twice that used in the preceding condensation.

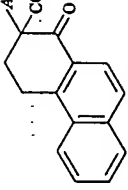
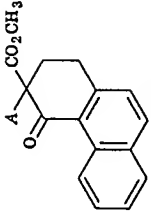
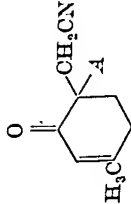
† Methyl chloroethyl ketone was employed.







‡ In this experiment the actual reagents used were the ester, acetone, and formaldehyde.

††† When the adduct was hydrolyzed, a 28% over-all yield of (±)-piperitone was obtained.

TABLE II—Continued

MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC KETONES

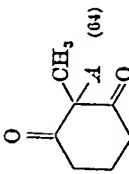
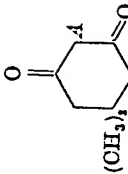
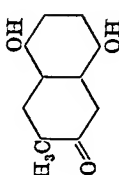
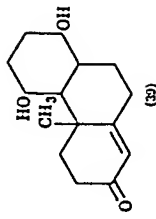
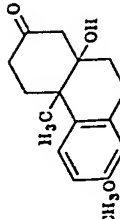
Reactants	Catalyst	Product, (Yield, %)	References
<i>Methyl Vinyl Ketone (Cont.) and</i>		$A = \text{CH}_3\text{COCH}_2\text{CH}_2-$	
Methyl 1-oxo-1,2,3,4-tetrahydro-phenanthrene-2-carboxylate	NaOCH_3	 (93)	532
Methyl 4-oxo-1,2,3,4-tetrahydro-phenanthrene-3-carboxylate	NaOCH_3	 (96)	533
Ethyl phenylpyruvate	Not indicated	3-Carboxy-3-hydroxy-2-methyl-4-phenyl-cyclohexanone	531
Malonitrile	NaOCH_3	$(A)_2\text{C}(\text{CN})_2$ (74)	119, 122
Benzyl cyanide	Na	$\text{C}_6\text{H}_5\text{CH}(A)\text{CN}$	121
Ethyl phenylcyanoacetate	Na	$\text{C}_6\text{H}_5\text{C}(A)(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (90)	121
Methyl β -cyanoethyl ketone	KCN		123

Acetone	—§ KOH,	3-Methyl-2-cyclohexen-1-one (3)	419
Isobutyraldehyde	—§ KOH,	4,4-Dimethyl-2-cyclohexen-1-one (40)	534
Methyl ethyl ketone	—§ KOH,	3,6-Dimethyl-2-cyclohexen-1-one (3)	419
Diethylacetaldehyde	—§ KOH,	4,4-Diethyl-2-cyclohexen-1-one	534
2-Ethylhexanal	—§ KOH,	4-n-Butyl-4-ethyl-2-cyclohexen-1-one	534
Cyclohexanone	Linamine from cyclohexanone	 (30-40)	535, 531
Phenylacetone	$[(C_6H_5CH_2N(CH_3)_2)OH]$	 and  (40)	536
Cyclohexane-1,3-dione	NaOCH ₃		532
	KOH, CH ₃ OH	 (39)	538
		 (36)	

Note. References 401-4015 are on pp. 545-555.

§ This experiment was run in the vapor phase, in the presence of oxides of group II to IV of the periodic system.
|| This was reported as the probable structure of the product.

TABLE II—Continued

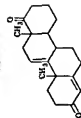
MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC KETONES			References
Reactants	Catalyst	Product (Yield, %)	
<i>Methyl Vinyl Ketone (Cont.) and</i>		$A = \text{CH}_3\text{COCH}_2\text{CH}_2\text{---}$	
2-Methylcyclohexane-1,3-dione	NaOCH_3 ; $(\text{C}_2\text{H}_5)_3\text{N}$	 (64)	525, 539
5,5-Dimethylcyclohexane-1,3-dione	KOH , CH_3OH	 (62)	538
5-Methyloctahydronaphthalene-1,6-dione	NaOCH_3	5-Methyl-5-(γ -ketobutyl)- $\Delta^{4a,8a}$ -octahydro-naphthalene-1,6-dione	115
	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	 (39)	540, 541
6-Methoxy-1-methyl-2-tetralone	Not indicated		531

3-Hydroxymethylene-4-keto-1,2,3,4-tetrahydrophenanthrene



533

and the 3-formyl derivative



NaOC_2H_5 ; *t*-amines

542

Nitromethane

$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$; $\Delta\text{CH}_3\text{NO}_2$ (51)

506, 523

Nitroethane

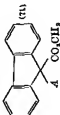
NaOCH_3 ,
 NaOCH_3

508

506, 543

$\text{CH}_3\text{CH}(\Delta)\text{NO}_2$ (49)
 $(\text{CH}_3)_2\text{C}(\Delta)\text{NO}_2$ (59)

Methyl fluorene-9-carboxylate

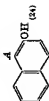


544

2-Naphthol

KOC_2H_5

168



Note: References 491-1045 are on pp. 545-555.

TABLE II—Continued
MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC KETONES


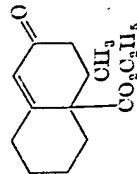
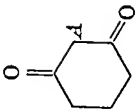
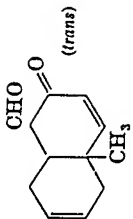
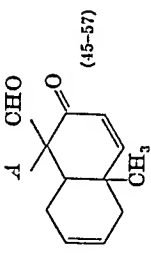
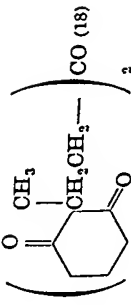


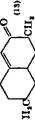
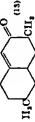
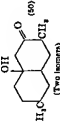
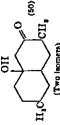
Reactants	Catalyst	Product (Yield, %)	References
<i>Methyl Vinyl Ketone (Cont.) and</i>			
Ethyl 3-hydroxybenzofuran-2-carboxylate	NaOC_2H_5	$A = \text{CH}_3\text{COCH}_2\text{CH}_3$ —  (90)	119
2'-Hydroxymethylene-1'-oxo-1',2',3',4'-tetrahydro-1,2-benz-3,4-acceperinaphthane	NaOCH_3	1'-Oxo-2'-(γ -oxobutyl)-1',2',3',4'-tetrahydro-1,2-benz-3,4-acceperinaphthane (70)	545
<i>Hydroxymethyleneacetone and</i>	KOC_4H_9 - <i>t</i>	1'-Oxo-2'-(γ -oxobutyl)-1',2',3',4'-tetrahydro-1,2-benz-3,4-acceperinaphthane (26)	545
Ethyl acetoneacetate	NaOC_2H_5	2-Hydroxy-4-methylbenzoic acid (55)	427
Diethyl acetone-1,3-dicarboxylate	NaOC_2H_5	Diethyl 2-hydroxy-4-methylisophthalate (49)	427
Nitromethane	$\text{CH}_3\text{COCH}=\text{CHONa}$	$\text{CH}_3\text{COCH}_2\text{CH}(\text{OCH}_2\text{CH}_2\text{NO}_2)_2$ (4)	546
Ethyl malonate [¶]	None	Ethyl 2-amino-6-methylnicotinate (32)	521
Cyanoacetamide	Piperidine acetate	3-Cyano-2-hydroxy-6-methylpyridine (55-62)	547
<i>Ethylidenacetone and</i>			
Diethyl methylmalonate	NaOC_2H_5	$A = \text{CH}_2\text{CH}(\text{CH}_3)\text{COCH}_3$ — 	422
Ethyl 2-oxocyclohexane-1-carboxylate	KOC_2H_5	2,3-Dimethylcyclohexane-1,5-dione (10)	409

TABLE II—Continued

MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC KETONES			References
Reactants	Catalyst	Product (Yield, %)	
<i>Ethyl Vinyl Ketone and</i> Diethyl malonate** Ethyl acetate** Acetylacetone**	NaOC_2H_5 NaOC_2H_5 NaOC_2H_5	$\text{A} = \text{CH}_3\text{CH}_2\text{COCH}_2\text{CH}_2-$ $\text{A} \text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ $\text{CH}_3\text{COCH}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}_3\text{COCH}(\text{A})\text{COCH}_3$	549 550 549
Cyclohexane-1,3-dione	Piperidine		537
 <i>Divinyl Ketone and</i>	KOC_4H_9-t	 (45-57)	551
2-Methylcyclohexane-1,3-dione	NaOCH_3	 (18)	538




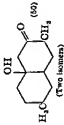
<i>Methyl Isopropenyl Ketone and</i>					
Ethyl acetoacetate	Na			$A = \text{CH}_3\text{COCH}(\text{CH}_3)\text{CH}_2-$	
Ethyl propionylacetate	Na			3,4-Dimethyl-2-cyclohexen-1-one	420
Ethyl isobutyrylacetate	KOH, $\text{C}_4\text{H}_9\text{OH}$			3-Ethyl-4-methyl-2-cyclohexen-1-one	420
Acetone	KOH, CH_3OH			$(\text{CH}_3)_2\text{CHCOCH}(\text{A})\text{CO}_2\text{C}_4\text{H}_9$ (75)	119
Methyl ethyl ketone	KOH, CH_3OH			3,6-Dimethyl-2-cyclohexen-1-one (20)	418, 552††
				3,4,6-Trimethyl-2-cyclohexen-1-one‡‡ (49, 43)	418, 552
Cyclohexanone	KOH, $\text{C}_4\text{H}_9\text{OH}$				309, 101
4-Methylcyclohexanone	KOH, $\text{C}_4\text{H}_9\text{OH}$				101, cf. 8
					

Note: References 401-1045 are on pp. 545-555.

** β Chloroethyl ethyl ketone was employed.

†† When 3-hydroxy-3-methylbutan-2-one was used, instead of the unsaturated ketone, the yield was 11%.

‡‡ The same product was obtained from methyl ethyl ketone and formaldehyde (49-52%) and from methyl ethyl ketone and 3-hydroxy-3-methylbutan-2-one (43-49%).

<i>Methyl Isopropenyl Ketone and</i>				
Ethyl acetacetate	Na	$A = CH_3COCH(OH)CH_3$ —		
Ethyl propionylacetate	Na	3,4-Dimethyl-2-cyclohexen-1-one	420	
Ethyl isobutyrylacetate	KOH, C_3H_7OH	3-Ethyl-4-methyl-2-cyclohexen-1-one	420	
Acetone	KOH, CH_3OH	$(CH_3)_2CHCOCH(A)CO_2C_2H_5$ (75)	119	
Methyl ethyl ketone	KOH, CH_3OH	3,6-Dimethyl-2-cyclohexen-1-one (20)	418, 552††	
		3,4,6-Trimethyl-2-cyclohexen-1-one‡‡ (49, 43)	418, 552	
Cyclohexanone	KOH, C_3H_7OH			369, 101
				
4-Methylcyclohexanone	KOH, C_3H_7OH			101, cf. 8
				

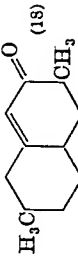
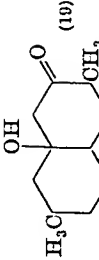
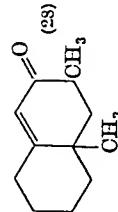
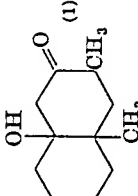
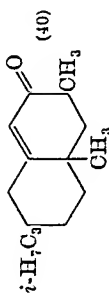
Note: References 491-1045 are on pp. 545-555.

** β -Chloroethyl ethyl ketone was employed.

†† When 3-hydroxy-3-methylbutan-2-one was used, instead of the unsaturated ketone, the yield was 11%.

‡‡ The same product was obtained from methyl ethyl ketone and formaldehyde (49-52%) and from methyl ethyl ketone and 3-hydroxy-3-methylbutan-2-one (43-49%).

TABLE II—Continued

MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC KETONES			References
Reactants	Catalyst	Product (Yield, %)	
<i>Methyl Isopropenyl Ketone (Cont.) and</i>		$A = \text{CH}_3\text{COCH}(\text{CH}_3)\text{CH}_2-$	
3-Methylcyclohexanone	KOH, $\text{C}_2\text{H}_5\text{OH}$	 (18)	101
		 (19) (Two isomers)	
2-Methylcyclohexanone	KOH, $\text{C}_2\text{H}_5\text{OH}$	 (23)	101
		 (1)	
Tetrahydrocurvone	KOH, $\text{C}_2\text{H}_5\text{OH}$	 (40)	101
<i>4-Hydroxy-3-penten-2-one and</i>			
Diethyl acetone-1,3-dicarboxylate	NaOC_2H_5	Diethyl 2-hydroxy-4,6-dimethylisophthalate (92)	427
Malonamide	None	4,6-Dimethyl-2-pyridone-3-carboxamide	370
Malononitrile	None	4,6-Dimethyl-3-cyano-2-pyridone	370

$H_2NC(=NH)CH_2CO_2C_2H_5$ ¶	None	Ethyl 2-amino-4,6-dimethylpyridine-3-carboxylate (50, 69)	514, 521
Cyanoacetamide	None	4,6-Dimethyl-2-pyridone 3-carboxamide	370
Cyanoacetamide§§	Piperidine	3 Cyano-4,6-dimethyl-2-pyridone (87, 100)	553, 371, 554
$NCCl_4CONHCH_3$ §§	NH_3	3-Cyano-4,6-dimethyl-2-pyridone	555
$NCCl_4CONHC_2H_5$ §§	CH_3NH_2	3 Cyano-1,4,6-trimethyl-2-pyridone	555
$NCCl_4CONHC_2H_5CH=CH_2$ §§	$C_2H_5NH_2$	3-Cyano-4,6-dimethyl-1-ethyl-2-pyridone	555
$CH_3COCH_2C(=NH)CH_2$ §§	$CH_2=CHCH_2NH_2$	1 Allyl 3-cyano-4,6-dimethyl-2-pyridone	555
	None	Methyl 2,4,6-trimethyl-3-pyridyl ketone (>75)	414
4-Amino-3-penten-2-one and			
Ethyl cyanoacetate	None	3-Cyano-4,6-dimethyl-2-pyridone	555
N-Methylcyanoacetamide	None	3-Cyano-1,4,6-trimethyl-2-pyridone	556
Methyl α -Hydroxymethylcneethyl Ketone and	Piperidine		
Cyanoacetamide		3 Cyano-4 hydroxy 5,6-dimethyl-2,3,4,5-tetrahydro 2-pyridone or 3-cyano-5,6 dimethyl-2-hydroxypyridine (23)	171, 172
$CH_3C(=NH)CH_2CO_2C_2H_5$	None	Ethyl 2,5,6-trimethylpyridine-3-carboxylate	557
3-Hydroxymethylcnepentane-2,4-dione and			
Cyanoacetamide	$NaOC_2H_5$	Compound $C_9H_8N_2O_2$	254
Mesityl Oxide and		$A = CH_3COCH_2C(CH_3)_2$	
Dimethyl malonate	$NaOCl_2$	4-Carbomethoxy-5,5-dimethylcyclohexane-1,3-dione (85)	558

Note. References 491-1015 are on pp. 545-555.

¶ The ester imino ether was used.

§§ A mixture of ethyl cyanoacetate and ammonia or the appropriate amine was used in these experiments.

TABLE II—Continued
MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC KETONES

Reactants	Catalyst	Product (Yield, %)	References
<i>Nesityl Oxide (Cont.) and</i>		$A = \text{CH}_3\text{COCH}_2\text{C}(\text{CH}_3)_2$	
Diethyl malonate	NaOC_2H_5	5,5-Dimethylcyclohexane-1,3-dione (67-85) or 4-carbethoxy-5,5-dimethylcyclohexane-1,3-dione (95-97)	558, 558a
Diethyl methylmalonate	NaOC_2H_5	4,5,5-Trimethylcyclohexane-1,3-dione	315
Ethyl phenylacetate	NaOC_2H_5	5,5-Dimethyl-4-phenylcyclohexane-1,3-dione	82
Ethyl acetoacetate	NaOC_2H_5	3,5,5-Trimethyl-2-cyclohexen-1-one (low)	15, 16, 17, cf. 119
Ethyl benzoylacetate	NaOC_2H_5	4-Carbethoxy-5,5-dimethyl-3-phenyl-2-cyclohexen-1-one (44)	414
Methyl cyanoacetate	Na	$\text{NCCH(A)CO}_2\text{OH}_3$	415
Ethyl cyanoacetate	NaOC_2H_5	4-Cyano-5,5-dimethylcyclohexane-1,3-dione (50)	415, 425
Cyanoacetamide	NaOC_2H_5	3-Cyano-6-hydroxy-4,4,6-trimethyl-2-piperidone (quant.)	559
Deoxybenzoin	NaOC_2H_5	$\text{C}_6\text{H}_5\text{COCH(A)C}_6\text{H}_5$ and 5,5-dimethyl-3,4-diphenyl-2-cyclohexen-1-one	414
Acetylacetone	Na	6-Acetyl-3,5,5-trimethyl-2-cyclohexen-1-one	415
Nitromethane	NaOC_2H_5	ACl_2NO_2 (83)	500
Fluorene	$(\text{C}_6\text{H}_5)_2\text{NH}$	ACl_2NO_2 (85)	209
4-Hydroxycoumarin	KOH, pyridine	5-(9-Fluorenyl)-4,4-dimethylpentan-2-one (15-20)	561
	Pyridine	4-(4-Hydroxycoumarinyl)-4-methylpentan-2-one (43)	169
3-Ethyl-3-buten-2-one and Methyl propyl ketone	KOH, CH_3OH	4,6-Diethyl-3-methyl-2-cyclohexenone (7, 20)	552, 418

3-Methyl-3-penten-2-one and Diethyl malonate	NaOC ₂ H ₅	4,5-Dimethylcyclohexane-1,3-dione*** (10)	422
2-Methyl-1-penten-3-one and Ethyl propionylacetate	Not indicated	2,4-Dimethyl-3-ethyl-2-cyclohexenone	420
Ethyl methylacetoacetate	Not indicated	3-Ethyl-4,6-dimethyl-2-cyclohexenone	420
Ethyl ethylacetoacetate	Not indicated	3,6-Diethyl-4-methyl-2-cyclohexenone	420
4-Hydroxy-3-methyl-3-penten-2-one and Cyanoacetamide §§	None	3-Cyano-4,5,6-trimethyl-2-pyridone	555
NCCH ₃ CONHCH ₃ §§	Piperidine	3-Cyano-4,5,6-trimethyl-2-pyridone	562, cf. 563
	None	3-Cyano-1,4,5,6-tetramethyl-2-pyridone	555
Ethyl α-Hydroxymethylmethyl Ketone and Cyanoacetamide	sec-Amine	3-Cyano-6-ethyl-2-hydroxy-5-methylpyridine	254
CH ₃ C(=NH)CH ₂ CO ₂ C ₂ H ₅	None	Ethyl 6-ethyl-2,5-dimethylpyridine-3-carboxylate (50)	442
CH ₃ C(=NH)CH ₂ COCH ₃	None	Methyl 6-ethyl-2,5-dimethyl-3-pyridyl ketone (46)	442
Nitromethane	CH ₃ CH ₂ COC. (=CHONa)CH ₃	5-Hydroxy 4-methyl 6-nitrohexan-3-one (51)	546
Methyl β-Ethoxymethyl Ketone and Cyanoacetamide	Piperidine	3-Cyano 6-methyl-2-pyridone (75)	564

Note. References 491-1045 are on pp. 545-555.

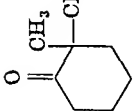
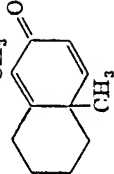
§§ A mixture of ethyl cyanoacetate and ammonia or the appropriate amine was used in these experiments.



||| A mixture of trioxymethylene and the ketone was used.

¶¶ The same product was obtained in 23% yield from the ketone and 3-ethyl-4-hydroxy-2-butanone, and in 20% yield from methyl propyl ketone and formaldehyde.

*** The name used in the reference is erroneous.

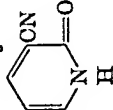
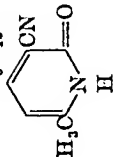
TABLE II—Continued

MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC KETONES		Product (Yield, %)		References
Reactants	Catalyst			
β -Methoxyvinyl Ethyl Ketone and				
2-Methylcyclohexanone	Na	  (Small) 380	505, 422	
3-Hepten-2-one and Diethyl malonate	NaOC ₂ H ₅		5-n-Propylcyclohexane-1,3-dione (16, 24)	
4-Methyl-3-hexen-2-one and Cyanoacetamide	NaOC ₂ H ₅		3-Cyano-4-ethyl-6-hydroxy-1,6-dimethyl-2-piperidone (63)	506
5-Methyl-3-hexen-2-one and Diethyl malonate	NaOC ₂ H ₅		5-Isopropylcyclohexane-1,3-dione (80)	422, 507, 508
3,4-Dimethyl-3-penten-2-one and Diethyl malonate	NaOC ₂ H ₅		4,5,5-Trimethylcyclohexane-1,3-dione	509
5-Hydroxy-4-hepten-3-one and Cyanoacetamide	None		3-Cyano-4,6-diethyl-2-pyridone	370
4-Hydroxy-5-ethoxy-3-penten-2-one and Cyanoacetamide	Piperidine		3-Cyano-4-ethoxymethyl-6-methyl-2-pyridone (81)	477

4-Hydroxy-3-ethyl 3-penten-2-one and Cyanoacetamide	None	3-Cyano-6-ethyl-4,6-dimethyl-2-pyridone	371
Methyl β -Isopropoxyvinyl Ketone and Diethyl malonate	Na	$\text{CH}_3\text{COCH}=\text{CHCH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ and 	380
Methyl 4-Oxo-5-hexenoate and			
2-Methylcyclohexane-1,3-dione	NaOCH_3		525
6-Methyl 4-hepten-3-one and Diethyl malonate	NaOC_2H_5	5 Isopropyl-2-methylcyclohexane-1,3-dione (43)	422
4-Ethyl-3-hexen-2-one and Diethyl malonate Cyanoacetamide	NaOC_2H_5 NaOC_2H_5	5,5-Diethylcyclohexane-1,3-dione (50) 3-Cyano-4,4-diethyl 6-hydroxy-6-methyl-2-piperidone (75)	570 566
n-Propyl β -Ethoxyvinyl Ketone and Cyanoacetamide	Piperidine	3-Cyano-6-n-propyl 2-pyridone (64)	564

Note: References 491-1045 are on pp. 545-555.

TABLE II—Continued

MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC KETONES		Catalyst	Product (Yield, %)	References
Reactants				
Isopropyl β -Ethoxyvinyl Ketone and Cyanacetamide		Piperidine	3-Cyano-6-isopropyl-2-pyridone (77)	564
3- <i>n</i> -Amyl-3-buten-2-one and Methyl hexyl ketone		KOH, CH ₃ OH	4,6-Di-(<i>n</i> -amyl)-3-methyl-2-cyclohexenone (23, 33)	418, 552
6-Methyl-5-nonen-4-one and Diethyl malonate		NaOC ₂ H ₅	2-Ethyl-5-methyl-5- <i>n</i> -propylcyclohexane-1,3-dione	571
Decane-2,4-dione (enol) and Cyanacetamide §§		None	<div style="display: flex; align-items: center; justify-content: center;"> <div style="text-align: center;"> CH_3  $n\text{-H}_{13}\text{C}_6$ </div> <div style="margin: 0 10px;">or</div> <div style="text-align: center;">  $\text{C}_6\text{H}_{13-n}$ </div> </div>	555
β -Ethoxyvinyl <i>n</i> -Amyl Ketone and Cyanacetamide		Piperidine	6- <i>n</i> -Amyl-3-cyano-2-pyridone (68)	534

8-Methyl-7-tridecen-6-one and Diethyl malonate	NaOC_2H_5	$A = n\text{-C}_6\text{H}_{11}\text{COCH}_2\overset{ }{\text{C}}(\text{CH}_3)\text{C}_6\text{H}_{11}\text{-}n$ 5- <i>n</i> -Amyl-2- <i>n</i> -butyl-5-methylcyclohexane-1,3- dione (80) $\text{ACH}(\text{CN})\text{CONH}_2$ (84)	572
Cyanoacetamide	NaOC_2H_5		572
1-Hydroxymethyleneheptadecan-2-one and Diethyl acetone-1,3-dicarboxylate	NaOC_2H_5	Diethyl 2-hydroxy-4- <i>n</i> -pentadecylsophthalate (52)	427
13-Methyl-12-tricosen-11-one and Diethyl malonate	NaOC_2H_5	$A = n\text{-C}_{19}\text{H}_{39}\overset{ }{\text{C}}(\text{CH}_3)\text{CH}_2\text{COC}_{10}\text{H}_{21}\text{-}n$	572
Cyanoacetamide	NaOC_2H_5	5- <i>n</i> -Decyl 5-methyl 2- <i>n</i> -nonylcyclohexane-1,3- dione (80) $\text{ACH}_2\text{CO}_2\text{C}_2\text{H}_5$ †††	572

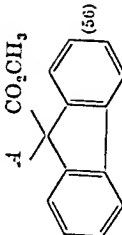
Note: References 491-1045 are on pp. 545-555.



§§ A mixture of ethyl cyanoacetate and ammonia or the appropriate amine was used in these experiments.

||| A mixture of trioxymethylene and the ketone was used.

††† This product was obtained after acid hydrolysis and esterification.

TABLE III

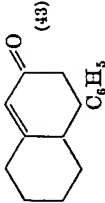
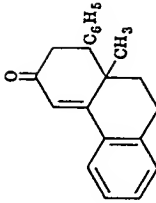
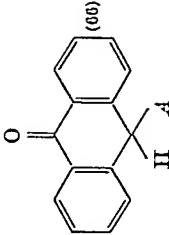
MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC KETONES			
Reactants	Catalyst	Product (Yield, %)	References
<i>Vinyl Phenyl Ketone</i> * and Dimethyl malonate	NaOCH ₃	$A = C_6H_5COCH_2CH_2-$ $A'CH(CO_2CH_3)_2$ (70), $(A')_2C(CO_2CH_3)_2$ (small)	573
Methyl fluorene-9-carboxylate	KOH		544
Ethyl acetoacetate	NaOC ₂ H ₅	6-Carbethoxy-3-phenyl-2-cyclohexen-1-one	574
Malononitrile	NaOCH ₃	$(A)_2C(CN)_2$	228
Methyl cyanoacetate	NaOCH ₃	$(A)_2C(CN)CO_2CH_3$ (70)	228
Cyanoacetamide	NaOCH ₃	$(A)_2C(CN)CONH_2$	228
Methyl benzyl ketone	NaOCH ₃	3,6-Diphenyl-2-cyclohexen-1-one	574
Deoxybenzoin	NaOCH ₃	$C_6H_5COCH(A)C_6H_5$ (60)	575
Dibenzyl ketone	NaOC ₂ H ₅	2,3,6-Triphenyl-2-cyclohexen-1-one	574
Benzyl p-biphenyl ketone	NaOCH ₃	$C_6H_5CH(A)COC_6H_4C_6H_5-p$	575
Nitromethane	NaOCH ₃	$(A)_3CNO_2$	228
Phenylnitromethane	NaOCH ₃	$C_6H_5CH(A)NO_2$ (82)	576
<i>Hydroxymethylphenacetophenone</i> and Ethyl acetoacetate	$[CH_3COCHCO_2C_2H_5]Na$	Ethyl 3-hydroxybiphenyl-4-carboxylate (42)	577
Diethyl acetone-1,3-dicarboxylate	NaOC ₂ H ₅	Diethyl 3-hydroxybiphenyl-2,4-dicarboxylate (50)	427
$CH_3C(=NH)CH_2COCH_3$	None	3-Acetyl-2-methyl-6-phenylpyridine	422
$CH_3C(=NH)CH_2COC_6H_5$	None	3-Benzoyl-2-methyl-6-phenylpyridine	442
Nitromethane	$C_6H_5COCH=CHONa$	β -Hydroxy- γ -nitrobutyrophenone	545
(<i>Methoxymethylene</i>)acetophenone and Ethyl acetoacetate	$[CH_3COCHCO_2C_2H_5]Na$	Ethyl 3-hydroxybiphenyl-4-carboxylate (42)	577

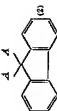
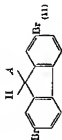

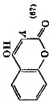
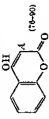
<i>Benzylidenacetone and</i>		$A = \text{CH}_2\text{COCH}_2\text{CHC}_6\text{H}_5$	
Dimethyl malonate	NaOCH ₃	ACH(CO ₂ CH ₃) ₂	71
Diethyl malonate	Na, NaOC ₂ H ₅	5-Phenylcyclohexane-1,3-dione (75) or its 4-carbethoxy derivative	4, 678 579
	KOH, acetal	ACH(CO ₂ C ₂ H ₅) ₂ (84)	483, 517, 518, 580, 30
Ethyl phenylacetate	NaOC ₂ H ₅	4,5-Diphenylcyclohexane-1,3-dione	82
Ethyl cyclopentanone-2-carboxylate	KOC ₂ H ₅		409
Ethyl cyclohexanone-2-carboxylate	KOC ₂ H ₅		409
Ethyl cyanoacetate	NaOC ₂ H ₅	ACH(CN)CO ₂ C ₂ H ₅ (91)	121
Ethyl α-cyanobutyrate	NaOC ₂ H ₅	CH ₃ CH ₂ C(A)(CN)CO ₂ C ₂ H ₅ (23)	581
Ethyl α-cyanoacrylate	NaOC ₂ H ₅	C ₆ H ₅ C(A)(CN)CO ₂ C ₂ H ₅ (78)	121
Cyanoacetamide	sec. Amine NaOC ₂ H ₅	3-Cyano-6-hydroxy-6-methyl 4-phenyl-2-piperidone 3-Cyano-2-keto-6 methyl-4-phenyl-2,3,4,5-tetra- hydropyridine	439
Acetonitrile	KOH, acetal	ACH ₂ CN (82)	439, 224
CH ₃ C(=NH)CH ₂ CN	NaOC ₂ H ₅	3-Cyano-2,6-dimethyl-4-phenylpyridine (12)	483, 517, 518
Benzyl cyanide	NaOCH ₃	C ₆ H ₅ CH(A)CN (87)	440
Deoxy benzoin	NaOC ₂ H ₅	C ₆ H ₅ COCH(A)C ₂ H ₅	121 416

Note. References 401-1045 are on pp 545-555

* β-Chloropropiophenone was actually used in these condensations.

TABLE III—Continued
MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC KETONES

Reactants	Catalyst	Product (Yield, %)	References
<i>Benzylidenecyclohexanone (Cont.) and</i>			
Cyclohexanone	NaNH_2	 <p>(43)</p> <p>$A = \text{CH}_3\text{COCH}_2\text{CHOC}_6\text{H}_5$</p>	98
2-Methyl-1-tetralone	NaNH_2		98
Anthrone	Piperidine	 <p>(66)</p>	582
Nitromethane	$(\text{C}_2\text{H}_5)_2\text{NH}$	$A\text{CH}_2\text{NO}_2$ (58)	200
1-Nitropropane	$(\text{C}_2\text{H}_5)_2\text{NH}$	$\text{CH}_3\text{CH}_2\text{CH}(A)\text{NO}_2$ (two isomers: total, 90)	200
2-Nitropropane	$(\text{C}_2\text{H}_5)_2\text{NH}$	$(\text{CH}_3)_2\text{C}(A)\text{NO}_2$ (77)	209
Ethyl nitroacetate	$(\text{C}_2\text{H}_5)_2\text{NH}$	$\text{O}_2\text{NCH}(A)\text{CO}_2\text{C}_2\text{H}_5$ (54)†	154
	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{OH}_3)_3]\text{OH}$	$\text{O}_2\text{NCH}(A)\text{CO}_2\text{C}_2\text{H}_5$	

Fluorene	NaOC_2H_5		370
2,7-Dibromofluorene	NaOC_2H_5		376
2-Hydroxy-1,4-naphthoquinone	Pyridine		583
4-Hydroxycoumarin	Piperidine		169, 584
Triethyl phosphonoacetate	NH_3 , <i>t</i> -amines NaOC_2H_5	 ($\text{C}_2\text{H}_5\text{O}$) ₂ P(O)CH(A)CO ₂ C ₂ H ₅ (48)	585 124



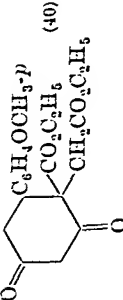
Note: References 491-1045 are on pp. 545-555.

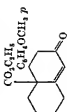

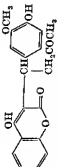
† The product was obtained as a salt of the *ac*i form.

TABLE III—Continued

MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC KETONES

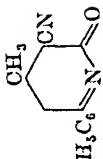
A. Substituted Benzylidenacetones

Substituent in	Addend	Catalyst	Product (Yield, %)	References
 2-Hydroxy	Ethyl acetoacetate	NaOC_2H_5	$A = \text{ArylCHCH}_2\text{COCH}_3$ 4-Acetyl-2-methyl-1,4-benzopyran 4-Acetyl-2,3-dimethyl-1,4-benzopyran (52) 4-Acetyl-2-methyl-3-phenyl-1,4-benzopyran	434 38 38
	Ethyl methylacetoacetate	NaOC_2H_5		
	Ethyl phenylacetoacetate	NaOC_2H_5		
2-Hydroxybenzylidenacetone		NaOC_2H_5	 2-HOC ₂ H ₅	586
2-Methoxy	Ethyl acetoacetate	Aq. NaOH	2 (or 4)-Carbethoxy-5-(<i>o</i> -methoxyphenyl)-3-methyl-2-cyclohexen-1-one	434
4-Methoxy	Diethyl malonate	NaOC_2H_5	5-(<i>o</i> -Methoxyphenyl)cyclohexane-1,3-dione	587
	Diethyl malonate	NaOC_2H_5	5-(<i>p</i> -Methoxyphenyl)cyclohexane-1,3-dione (59)	587
	Ethyl acetoacetate	Piperidine	$\text{CH}_3\text{COCH}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (55)	588
Triethyl ethane-1,2,2-tricarboxylate		NaOC_2H_5	 (40)	109

Ethyl cyclopentanone-2-carboxylate	KOC_2H_5	$\text{CH}_3\text{COCH}_2\text{CH}(\text{C}_6\text{H}_4\text{OCH}_2-p)\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)-\text{CH}_2\text{CH}_2\text{CO}_2\text{H}$	409
Ethyl cyclohexanone-2-carboxylate	KOC_2H_5		409
Ethyl cyanoacetate	NaOC_2H_5	4-Cyano-5-(<i>p</i> -methoxyphenyl)cyclohexane-1,3-dione (90)	589
Deoxybenzoin	NaOC_2H_5	$\text{C}_6\text{H}_5\text{COCH}(\text{A})\text{C}_6\text{H}_5$	589 416
4-Hydroxycoumarin	Pyridine		169
Diethylmalonate	NaOC_2H_5	5-(<i>m</i> -Nitrophenyl)cyclohexane-1,3-dione	590
Diethyl malonate	NaOC_2H_5	5-(<i>p</i> -Nitrophenyl)cyclohexane-1,3-dione	590
Diethyl malonate	NaOC_2H_5	5-(<i>o</i> -Chlorophenyl)cyclohexane-1,3-dione (27)	587
4-Hydroxy-3-methoxy 4-Hydroxycoumarin	Pyridine		169
Ethyl α-cyanobutyrate	NaOC_2H_5	$\text{CH}_3\text{CH}_2\text{C}(\text{CN})(\text{A})\text{CO}_2\text{C}_2\text{H}_5$	581
Ethyl acetoacetate	Aq NaOH	2 Carbethoxy-3-(<i>p</i> -dimethylaminophenyl)-5-hydroxy 5-methylcyclohexan-1-one	285
Diethyl malonate	NaOC_2H_5	5-(<i>p</i> -Isopropylphenyl)cyclohexane 1,3-dione (90)	578

Note: References 491-1045 are on pp 545-555

TABLE III—Continued
MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC KETONES

Reactants	Catalyst	Product (Yield, %)	References
<i>Ethylidenacetophenone and</i>			
Cyanoacetamide	NaOC_2H_5		591
<i>Hydroxymethylene-p-methylacetophenone and</i>			
$\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	None	Ethyl 2-methyl-6-(p-tolyl)pyridine-3-carboxylate	557
$\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{COCH}_3$	None	3-Acetyl-2-methyl-6-(p-tolyl)pyridine	442, 557
$\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{COC}_6\text{H}_5$	None	3-Benzoyl-2-methyl-6-(p-tolyl)pyridine	442
<i>α-Hydroxymethylencethyl Phenyl Ketone and</i>			
$\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	None	Ethyl 2,5-dimethyl-6-phenylpyridine-3-carboxylate	557
<i>Benzoylacetone (Enol) and</i>			
Diethyl acetone-1,3-dicarboxylate	NaOC_2H_5	Diethyl 3-hydroxy-5-methylbiphenyl-2,4-dicarboxylate (47)	427
Cyanoacetamide	$(\text{C}_2\text{H}_5)_2\text{NH}$	3-Cyano-6-methyl-4-phenyl-2-pyridone and 3-cyano-4-methyl-6-phenyl-2-pyridone	371, 592
Ethyl cyanoacetate	$(\text{C}_2\text{H}_5)_2\text{NH}$	3-Carboethoxy-4-methyl-6-phenyl-2-pyridone (low)	370
Malononitrile	$(\text{C}_2\text{H}_5)_2\text{NH}$	3-Cyano-4-methyl-6-phenyl-2-pyridone	370
<i>3-Amino-1-phenyl-2-buten-1-one and</i>			
Malonamide	None	2-Hydroxy-4-methyl-6-phenylpyridine-3-carboxamide	391, 398
Ethyl cyanoacetate	NaOC_2H_5	3-Cyano-6-methyl-4-phenyl-2-pyridone	391
Cyanoacetamide	None	3-Cyano-4-methyl-6-phenyl-2-pyridone	391

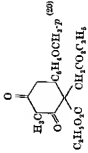
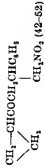
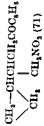
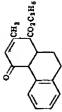
$\text{NCCl}_2\text{CONHCl}$	None	3-Cyano-1,4-dimethyl-6-phenyl-2-pyridone and 3-cyano-4-methyl-6-phenyl-2-pyridone	391
<i>Ethyl Styryl Ketone and</i> Diethyl malonate	NaOC_2H_5	4-Carbethoxy-2-methyl-5-phenylcyclohexane- 1,3-dione (70)	423
Ethyl phenylacetate	NaOC_2H_5	2-Methyl-5-phenyl-cyclohexane-1,3-dione (80) 2-Methyl-4,5-diphenylcyclohexane-1,3-dione (21, 32)	422 423, 422
<i>Ethyl Phenacyl Ketone (Enol) and</i> Cyanacetamide	None	3-Cyano-4-ethyl-6-phenyl-2-pyridone	371
1-Hydroxy-5-phenyl-1-penten-3-one and Cyanacetamide	Piperidine	$\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}$, 5-cyano-6-hydroxy-2-phenethyl- pyridine (?)	172
1-Phenyl-2-methyl-2-buten-1-one and Nitromethane	NaOC_2H_5	$\text{C}_6\text{H}_5\text{COCH}(\text{CH}_3)\text{CH}(\text{CH}_3)\text{CH}_2\text{NO}_2$ (63)	560
1-Phenyl-3-methyl-2-buten-1-one and Nitromethane	NaOC_2H_5	$\text{C}_6\text{H}_5\text{COCH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{NO}_2$ (70)	560
5-Phenyl-3-penten-2-one† and Diethyl malonate	NaOC_2H_5	5-Benzylcyclohexane-1,3-dione	593
4-Phenyl-4-methoxy-3-buten-2-one and Cyanacetamide	NaOC_2H_5 ; $(\text{C}_2\text{H}_5)_3\text{NNH}$	3-Cyano-6-methyl-4-phenyl-2-pyridone (90)	592
1-Phenyl-3-ethoxy-2-buten-1-one and Cyanacetamide	NaOC_2H_5	3-Cyano-4-methyl-6-phenyl-2-pyridone	592

Note: References 491-1015 are on pp. 545-555.

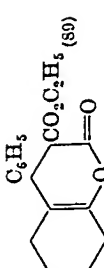
† This ketone was produced *in situ* by isomerization of 5-phenyl-4-penten-2-one.

TABLE III—Continued
MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC KETONES

Reactants	Catalyst	Product (Yield, %)	References
<i>p</i> -Methylbenzoylacetone (Enol) and Cyanoacetamide	$(C_2H_5)_2NH$	3-Cyano-4-methyl-6- <i>p</i> -tolyl-2-pyridone (80) and 3-cyano-6-methyl-4- <i>p</i> -tolyl-2-pyridone (in small amount from the isomeric enol)	594
$NCCH_2CONHCH_3$	$(C_2H_5)_2NH$	3-Cyano-1,6-dimethyl-4- <i>p</i> -tolyl-2-pyridone	594
1-Phenyl-3-methylamino-2-buten-1-one and Cyanoacetamide		3-Cyano-4-methyl-6-phenyl-2-pyridone and 3-cyano-1,4-dimethyl-6-phenyl-2-pyridone	391
Ethoxymethylcyclohexenone and Diethyl malonate	Na enolate of the ester	Ethyl 6-phenylcoumalin-3-carboxylate (44)	577
<i>n</i> -Propyl Styryl Ketone and Diethyl malonate	$NaOC_2H_5$	4-Carbethoxy-2-ethyl-5-phenylcyclohexane-1,3- dione (41)	423
Isopropyl Styryl Ketone and Diethyl malonate	$NaOC_2H_5$	$(CH_3)_2CHCOCH_2CH(C_6H_5)CH(CO_2C_2H_5)_2$ (79)	319
Ethyl <i>p</i> -Methoxystyryl Ketone and Diethyl malonate	$NaOC_2H_5$	4-Carbethoxy-5-(<i>p</i> -methoxyphenyl)-2-methylcyclo- hexane-1,3-dione (44)	595
Ethyl cyanoacetate	$NaOC_2H_5$	4-Cyano-5-(<i>p</i> -methoxyphenyl)cyclohexane-1,3- dione (55)	589

Triethylethane-1,1,2-tricarboxylate	NaOC_2H_5		
Cyclopropyl Styryl Ketone and Nitromethane	NaOCH_3		109
1-Phenyl 3-cyclopropyl-2-propen-1-one and Nitromethane	NaOCH_3		138
1-Acetyl-3,4-dihydronaphthalene and Ethyl acetate	NaOC_2H_5		138
3-Acetyl-4-phenyl-3-buten-2-one and Phenylnitromethane	$(\text{C}_2\text{H}_5)_4\text{NH}$		596
n-Butyl Styryl Ketone and Diethyl malonate	NaOC_2H_5	3-Acetyl-4,5-diphenyl-5-nitropentan-2-one (84)	29
		4-Carboxy-5-phenyl-2-n-propylcyclohexane-1,3-dione (35)	423

Note: References 491-1045 are on pp. 645-555.

TABLE III—Continued			
MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC KETONES			
Reactants	Catalyst	Product (Yield, %)	References
<i>Vinyl p-n-Propoxyphenyl Ketone and</i>		$A = p\text{-}n\text{-C}_3\text{H}_7\text{OC}_6\text{H}_4\text{COCH}_2\text{CH}_2\text{—}$	
Nitromethane	NaOH	(A) ₂ CHNO ₂ (73)	597
Phenylnitromethane	NaOCH ₃	C ₆ H ₅ CH(A)NO ₂ (71)	597
Cyanoacetamide	NaOCH ₃	NCC(A) ₂ CONH ₂ (83)	597
<i>Benzalpinacolone and</i>		$A = (\text{CH}_3)_2\text{CCOCH}_2\text{CHC}_6\text{H}_5$	
Dimethyl malonate	NaOCH ₃	ACH(CO ₂ CH ₃) ₂ (82)	598
Diethyl malonate	NaOC ₂ H ₅	ACH(CO ₂ C ₂ H ₅) ₂ (97, 70§)	598, 599
Methyl <i>p</i> -nitrophenylacetate	NaOCH ₃	<i>p</i> -O ₂ NC ₆ H ₄ CH(A)CO ₂ CH ₃	600
Ethyl <i>p</i> -nitrophenylacetate	NaOC ₂ H ₅	<i>p</i> -O ₂ NC ₆ H ₄ CH(A)CO ₂ C ₂ H ₅	600
Nitromethane	NaOCH ₃	ACH ₂ NO ₂ (80–90)	601
<i>Isopropyl p-Methoxystyryl Ketone and</i>			
Diethyl malonate	Enolate	(CH ₃) ₂ CHCOCH ₂ CH(C ₆ H ₄ OCH ₃ - <i>p</i>)CH ₂ CO ₂ H	30
<i>3-Ethoxy-1-p-tolyl-2-buten-1-one and</i>			
Cyanoacetamide	(C ₂ H ₅) ₂ NH	3-Cyano-4-methyl-6- <i>p</i> -tolyl-2-pyridone (quant.)	594
<i>2-Benzylidenecyclohexanone and</i>			
Diethyl malonate	Enolate		602
	Enolate	Ethyl β -(2-oxocyclohexyl)hydrocinnamate (70)	603

Diethyl malonate

Na

n-Heptyl Styryl Ketone and
Diethyl malonate

NaOC₂H₅

1,2-Diphenyl-2-propen-1-one and
Benzyl *p*-chlorophenyl ketone

KOH, CH₃OH

Benzyl *p*-tolyl ketone

KOH, CH₃OH

Benzyl *p*-anisyl ketone

KOH, CH₃OH

Deoxybenzoin

KOH, CH₃OH

Phenyl *p*-chlorobenzyl ketone

KOH, CH₃OH

Phenyl *p*-methylbenzyl ketone

KOH, CH₃OH

Phenyl *p*-dimethylaminobenzyl
ketone

KOH, CH₃OH

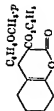
*D*ibenzoylmethane (Enol) and
Cyanoacetamide

NaOC₂H₅
(C₂H₅)₄NH
Piperidine

Vinyl *p*-Biphenyl Ketone and
Deoxybenzoin

NaOCH₃

Note: References 491-1045 are on pp. 545-555.
§ The acid was isolated in this experiment



602

4-Carbethoxy-2-pentyl-5-phenylcyclohexane-
1,3-dione (45)

423

$A = C_6H_5COCH(C_2H_5)CH_2-$
 $C_6H_5CH(A)COC_2H_5Cl-p$ (88)

604.

cf. 605, 606

$C_6H_5CH(A)COC_2H_5CH_2-p$ (85)

$C_6H_5CH(A)COC_2H_5OCH_2-p$ (74)

$C_6H_5CH(A)COC_2H_5$ (80)

$p-ClC_6H_4CH(A)COC_2H_5$ (77)

$p-CH_3C_6H_4CH(A)COC_2H_5$ (71)

$p-(CH_3)_3NC_6H_4CH(A)COC_2H_5$ (86)

604

604

604

604

604

604

604

3-Cyano-4,0-diphenyl-2-pyridone (5-20)

3-Cyano-4,0-diphenyl-2-pyridone (55-70)

3-Cyano-4,0-diphenyl-2-pyridone

370, 592

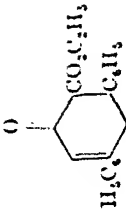
370, 592

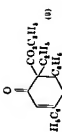
370, 592

$p-C_6H_5C_6H_4COCH_2CH_2CH(C_6H_5)COC_2H_5$

675

TABLE III—Continued
MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC KETONES

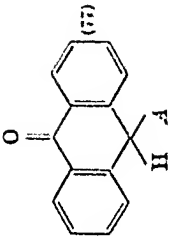
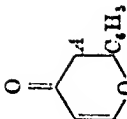
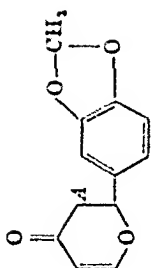
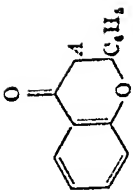
Reactants	Catalyst	Product (Yield, %)	References
<i>Chalcone</i> , $C_6H_5\dot{C}H=CHCOC_6H_5$, and		$A = C_6H_5\dot{C}HCH_2COC_6H_5$	
Dimethyl malonate	NaOCH ₃ Piperidine	$A\dot{C}H(CO_2CH_3)_2$ (80, 94)	75, 101 71
Diethyl malonate	Piperidine; 0.1 equiv. NaOC ₂ H ₅ ; KOH, acetal 1 equiv. NaOC ₂ H ₅	$A\dot{C}H(CO_2CH_2)_2$ (poor) $A\dot{C}H(CO_2C_2H_5)_2$ (71, 93, 98)	30, 55, 125, 483, 517, 518 55
Diethyl methylmalonate	Piperidine, NaOC ₂ H ₅ Na	Diethyl 5-benzoyl-2,1,6-triphenyl-1 cyclohexenyl-1,1-dicarboxylate (70) $A\dot{C}(CH_3)(CO_2C_2H_5)_2$ (80)	55, 125, 51 396, 607
Diethyl ethylmalonate	NaOC ₂ H ₅	Retrogression products	125
Diethyl phenylmalonate	NaOC ₂ H ₅	$A\dot{C}(C_6H_5)(CO_2C_2H_5)_2$ (94)	103
Diethyl succinate	NaOC ₂ H ₅	$A\dot{C}HCO_2H$ \mid CH_2CO_2H	73
Methyl phenylacetate	NaOCH ₃	$C_6H_5\dot{C}H(A)CO_2CH_3$	163, 608
Ethyl phenylacetate	NaOC ₂ H ₅	$C_6H_5\dot{C}H(A)CO_2C_2H_5$ (92); compound $C_6H_5O_4$	82, 125
Ethyl α -phenylbutyrate	NaOC ₂ H ₅	$C_6H_5\dot{C}(C_2H_5)(CO_2C_2H_5)_2$ (3)	125
<i>p</i> -O ₂ NC ₆ H ₄ CH ₂ CO ₂ CH ₃	NaOCH ₃	<i>p</i> -O ₂ NC ₆ H ₄ $\dot{C}H(A)CO_2CH_3$ (95)	640
<i>p</i> -O ₂ NC ₆ H ₄ CH ₂ CO ₂ C ₂ H ₅	NaOC ₂ H ₅	<i>p</i> -O ₂ NC ₆ H ₄ $\dot{C}H(A)CO_2C_2H_5$	606
<i>p</i> -O ₂ NC ₆ H ₄ CH ₂ CO ₂ C ₄ H ₉ - <i>n</i>	NaOC ₂ H ₅	<i>p</i> -O ₂ NC ₆ H ₄ $\dot{C}H(A)CO_2C_4H_9$ - <i>n</i>	600
Ethyl acetoacetate	NaOC ₂ H ₅ ; piperidine		125, cf. 19

$\text{CH}_3\text{COCH}(\text{C}_2\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5$	NaOC_2H_5		125
Ethyl benzoylacetate	Piperidine, NaOC_2H_5	$\text{C}_6\text{H}_5\text{COCH}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (91)	125
$\text{C}_6\text{H}_5\text{COCH}_2\text{CH}(\text{C}_6\text{H}_5)\text{CH}(\text{C}_6\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5$	Na in C_2H_5	Compound $\text{C}_{18}\text{H}_{14}\text{O}_6$	403
Methyl cyanoacetate	NaOCH_3	$\text{ACH}(\text{CN})\text{CO}_2\text{CH}_3$ and $(\text{A})_2\text{C}(\text{CN})\text{CO}_2\text{CH}_3$ (b,3)	609
Ethyl cyanoacetate	NaOC_2H_5	$(\text{A})_2\text{C}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (91)	121
Ethyl n-butyrylcyanoacetate	NaOC_2H_5	$\text{AC}(\text{C}_4\text{H}_9)\text{CN}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (78)	121
Cyanoacetamide	NaOCH_3	$\text{ACH}(\text{CN})\text{CONH}_2$ (72)	610
	Piperidine or $(\text{C}_2\text{H}_5)_2\text{NH}$	3-Cyano-8-hydroxy-4,6-diphenyl-2-piperidone (75)	439
	1 equiv. NaOC_2H_5	3-Cyano-1,6-diphenyl-3,4-dihydro-2-pyridone (87)	439
$\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CN}$	NaOC_2H_5	5-Cyano-6-methyl-2,4-diphenylpyridine and its 1,4-dihydro derivative	440
Malononitrile	NaOCH_3	$\text{ACH}(\text{CN})_2$	610
Benzyl cyanide	NaOCH_3	$\text{C}_6\text{H}_5\text{CH}(\text{A})\text{CN}$ (two isomers: 87; 40 and 30)	72, 611
Phenylacetaldehyde	NaOCH_3	$\text{C}_6\text{H}_5\text{C}(\text{A})_2\text{CN}$ (91)	612
Diethyl ketone	NaOCH_3	$\text{C}_6\text{H}_5\text{CH}(\text{OH})\text{CH}_2\text{CH}(\text{C}_6\text{H}_5)\text{CH}(\text{C}_6\text{H}_5)\text{CO}_2\text{H}$ (30)	163
Pinacolone	NaOC_2H_5	$\text{CH}_3\text{CH}(\text{A})\text{COC}_2\text{H}_5$ and $\text{CH}_3\text{C}(\text{A})_2\text{COC}_2\text{H}_5$ (90-100)	207
Acetophenone	NaOC_2H_5	$(\text{CH}_3)_2\text{CCOCH}(\text{A})_2$ (69)	207
Propiophenone	NaOC_2H_5	$\text{C}_6\text{H}_5\text{COCH}(\text{A})_2$ (27) and $\text{C}_6\text{H}_5\text{COC}(\text{A})_2$ (25)	125
n-Butyrophenone	NaOC_2H_5	$\text{CH}_3\text{CH}(\text{A})\text{COC}_2\text{H}_5$ (51) and $\text{CH}_3\text{C}(\text{A})_2\text{COC}_2\text{H}_5$ (27)	207
Isobutyrophenone	NaOC_2H_5	$\text{CH}_3\text{CH}_2\text{CH}(\text{A})\text{COC}_2\text{H}_5$ (19) and $\text{CH}_3\text{CH}_2\text{C}(\text{A})_2\text{COC}_2\text{H}_5$ (58)	207
Deoxybenzoin	NaOC_2H_5	$(\text{CH}_2)_2\text{C}(\text{COC}_2\text{H}_5)_2\text{CH}(\text{C}_6\text{H}_5)\text{CH}(\text{A})\text{COC}_2\text{H}_5$ (30)	207
Dibenzoylmethane	NaOC_2H_5	$\text{C}_6\text{H}_5\text{CH}(\text{A})\text{COC}_2\text{H}_5$ ($\text{C}_6\text{H}_5\text{CO})_2\text{CH}_2$ (1)	13 125

Note: References 491-1045 are on pp. 545-555.

|| Two isomeric acids and a non-acidic product, $\text{C}_{18}\text{H}_{14}\text{O}_6$, of unknown structure were obtained.

TABLE III—Continued

MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC KETONES			References
Reactants	Catalyst	Product (Yield, %)	
Chalcone, $C_6H_5CH=CHCOC_6H_5$, (Cont.) and		$A = C_6H_5CHCH_2COC_6H_5$	
Anthrone	$NaOCH_3$; NaOH, ethanol; <i>sec</i> -amines	 (77)	103, 013
2-Phenyl-2,3-dihydro- γ -pyrone	NaOH, ethanol		014
2-(3',4'-Methylenedioxyphenyl)- 2,3-dihydro- γ -pyrone	Na		014
2-Phenyl-2,3-dihydrobenzo- γ - pyrone	Aq. NaOH; $NaNH_2$; Na		015

Cyclopentanone

NaOH, ethanol;
(C₄H₉)₄NH

616



Cyclohexanone

NaOH, ethanol

613, 617



NaOC₄H₉

613

Compound C₁₄H₂₄O₂



3-Methylcyclohexanone

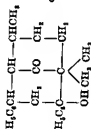
NaOH, ethanol;
piperidine

613, 616

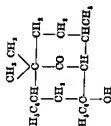
Menthone

NaOC₄H₉

616

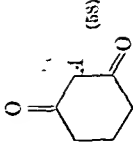

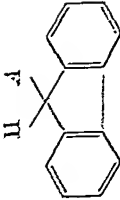


or



Note: References 491-1015 are on pp. 545-555.

TABLE III—Continued

MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC KETONES		
Reactants	Catalyst	Product (Yield, %)
<i>Chalcone</i> , $C_6H_5CH=CHCOC_6H_5$, (Cont.) and		$A = C_6H_5CHCH_2COC_6H_5$
Cyclohexane-1,3-dione	Piperidine	 (58)
Nitromethane	$NaOCH_3$; NH_3 , ethanol $(C_2H_5)_2NH$	ACH_2NO_2 (75, 88) and $(A)_2CHNO_2$ (small) $(A)_3CHNO_2$ (two isomers, 77)
Nitroethane	C_6H_5 , CH_3OH	ACH_2NO_2 (85-92)
1-Nitropropane	$(C_2H_5)_2NH$; $NaOCH_3$ $(C_2H_5)_2NH$	$CH_3CH(A)NO_2$ (two isomers: 78 + 11; quant.) $CH_3CH_2CH(A)NO_2$ (97)
2-Nitropropane	C_6H_5 , CH_3OH $(C_2H_5)_2NH$; $NaOCH_3$; CaH_2 , CH_3OH	$CH_3CH_2CH(A)NO_2$ (85-92) $(CH_3)_2C(A)NO_2$ (92-96)
Ethyl nitroacetate	$(C_2H_5)_2NH$	$O_2NCH(A)CO_2C_2H_5$ (94)
Benzyl <i>p</i> -tolyl sulfone	$NaOCH_3$	$C_6H_5CH(A)SO_2C_6H_4CH_3-p$ (two isomers: 15, 11)
Cyclopentadiene	Na derivative; piperidine	 $CH(C_6H_5)CH(A)COC_6H_5$ (small)
Fluorene	Pyridine, $NaOH$, H_2O	 (Quant.)

618

620, 209, 619

621

466a

209, 620

209

466a

209, 106a,

620

622

74

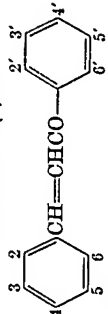

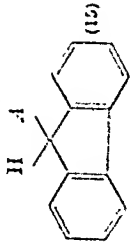
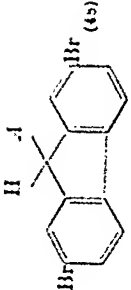
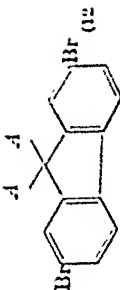
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
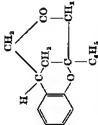
362, 623

NaOC_6H_5	 (10-27)	376
NaOC_2H_5	 (22)	376
4-Hydroxycoumarin	 (37)	169
2-Methylpyridine	Tri- and tetra-molecular condensation products	374
2-Methylquinoline	 (37) or  (60)	374
4-Methylquinoline	 (37)	374

Note: References 491-1045 are on pp. 545-555.

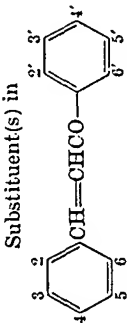
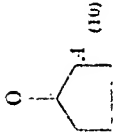
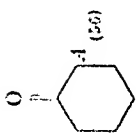
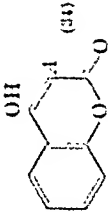
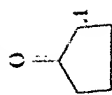
TABLE III—Continued
MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC KETONES
B. Substituted Chalcones





Substituent(s) in	Addend	Catalyst	Product (Yield, %)	References
	3-Br 4-Br 4'-Br	CH_3NO_2 CH_3NO_2 $\text{CH}_2(\text{CO}_2\text{CH}_3)_2$ $\text{CH}_2(\text{CO}_2\text{C}_2\text{H}_5)_2$ CH_3NO_2 1,4-Pentadiene	$\text{A} = \text{Appropriately Substituted}$ $\text{C}_6\text{H}_4\text{CHCH}_2\text{COC}_2\text{H}_5$ 	621 621 624 624 625 370
		NaOCH_3 NaOCH_3 NaOCH_3 NaOC_2H_5 NaOC_2H_5 NaOC_2H_5 ; NaNH_2 , liq. NH_3	ACH_2NO_2 ACH_2NO_2 $\text{ACH}(\text{CO}_2\text{CH}_3)_2$ (82) $\text{ACH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ ACH_2NO_2 (87) $(\text{CH}_2=\text{CH})_2\text{CH}_2\text{A}$ (4) $(\text{CH}_2=\text{CH})_2\text{CH}_2\text{A}$ (11)	
Fluorene		NaOC_2H_5		370
2,7-Dibromofluorene		NaOC_2H_5	 and 	370

4'-Cl	$\text{CH}_3(\text{CO}_2\text{CH}_3)_2$ $\text{NCCCH}_2\text{CO}_2\text{CH}_3$ $\text{CH}_3\text{CH}(\text{CN})\text{CO}_2\text{CH}_3$	NaOCH_3 NaOCH_3 NaOCH_3	$\Delta\text{CH}(\text{CO}_2\text{CH}_3)_2$ $\text{NCCCH}(\Delta)\text{CO}_2\text{CH}_3$ (87) $\text{CH}_3\text{C}(\text{CN})\text{CO}_2\text{CH}_3$ —A	609 609 609
	Cyclohexanone	NaOH , ethanol		613
2-HO	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	NaOC_2H_5		530, cf. 202, 203
	$\text{CH}_3\text{COCH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}_3\text{COCH}(\text{C}_6\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5$ $\text{C}_6\text{H}_5\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	NaOCH_3 NaOC_2H_5 Aq. NaOH	2,3-Dimethyl-4-phenacyl-1,4-benzopyran 2-Methyl-4-phenacyl-3-phenyl-1,4-benzopyran 4-Phenacyl-2-phenyl-1,4-benzopyran $\text{C}_6\text{H}_5\text{CH}(\Delta)\text{COC}_6\text{H}_5$ (95)	38 38 434 626

Note: References 491-1015 are on pp. 545-555.


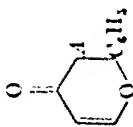
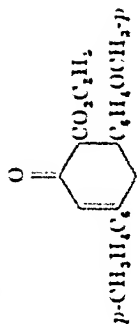
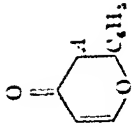
TABLE III—Continued





MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC KETONES				
Substituent(s) in	Addend	Catalyst	Product (Yield, %)	References
			$A =$ Appropriately Substituted $C_6H_5CHCH_2COC_6H_5$	
2-HO (Cont.)	Cyclopentanone	$(C_2H_5)_2NH$	 (10)	626
	Cyclohexanone	NaOH, ethanol	 (50)	626
2'-HO	4-Hydroxycoumarin	Pyridine	 (34)	109
4-CH ₃ O	$CH_2(CO_2CH_3)_2$ $CH_3COCH_2CO_2C_2H_5$ $NCCH_2CONH_2$	$NaOCH_3$ $NaOC_2H_5$ Na enolate	$A = CH(CO_2CH_3)_2$ (good) 2-Carbethoxy-3- <i>p</i> -methoxyphenyl-5-phenyl-5-cyclohexen-1-one 3-Cyano-2-hydroxy-4- <i>p</i> -methoxyphenyl-6-phenyl-1,5-dihydro-pyridine	627 628 594
	Cyclopentanone	sec-Amines		616

4'-ClH ₉	3-Methylcyclohexanone	<i>sec</i> -Amines; KOH, C ₂ H ₅ OH	 (Two isomers)	616
	Iodoxybenzoin	KOH, CH ₃ OH; NaOCH ₃	C ₆ H ₅ CH(A)COC ₆ H ₅ (42, little)	604, 620
	Nitromethane	NaOCH ₃	(A) ₂ CHNO ₂	621
	2-Phenyl-2,3-di- hydro-γ-pyrone	NaOC ₂ H ₅		614
3'-ClH ₉	Cyclohexanone	NaOH, ethanol		613
4-CH ₃	CH ₃ NO ₂	NaOCH ₃	(A) ₂ CHNO ₂	621
	2-Phenyl 2,3-di- hydro-γ-pyrone	NaOH, ethanol		614
4'-CH ₃	CH ₃ COCH ₂ CO ₂ C ₆ H ₅	NaOC ₂ H ₅	2-Carbethoxy-3-methyl-5- <i>p</i> tolyl- 5-cyclohexen-1-one	630

Note: References 491-1045 are on pp. 545-555.

TABLE III—Continued
MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC KETONES

Substituent(s) in	Addend	Catalyst	Product (Yield, %)	References
 4'-CH ₃ (Cont.)	NCCH ₂ CONH ₂	Piperidine	3-Cyano-6-hydroxy-4-phenyl-6- <i>p</i> -tolyl-2-piperidone (75)	439
3-NO ₂ 3-Br, 4-CH ₃ O	CH ₃ NO ₂ CH ₂ (CO ₂ CH ₃) ₂	NaOC ₂ H ₅ NaOC ₂ H ₅	3-Cyano-2-keto-4-phenyl-6- <i>p</i> -tolyl-2,3,4,5-tetrahydropyridine (90)	439
			(4), CHNO ₂ ACH(CO ₂ CH ₃) ₂	621 627
4,4'-Dimethoxy	2-Phenyl-2,3-dihydro- γ -pyrone	Na		614
4-CH ₃ O, 4'-CH ₃	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	NaOC ₂ H ₅		628
	2-Phenyl-2,3-dihydro- γ -pyrone	Na		614


3,4-Methylenedioxy	Cyclopentanone	sec-Amines		616
				
			<i>A</i>	
				616
	3-Methylcyclohexanone	sec-Amines; KOH, C ₂ H ₅ OH		
			(Two isomers)	
			<i>A</i>	
			ACH ₃ NO ₂ and (<i>A</i>) ₂ CHNO ₂	621
		NaOCH ₃		
Reactants	Catalyst	Product (Yield, %)		References
<i>α</i> -Bromobenzylidenecyclophenone and p-O ₂ NC ₆ H ₄ CH ₂ CN		$\text{H}_2\text{C}=\text{CH}-\text{C}(\text{CN})\text{C}_6\text{H}_4\text{NO}_2$	<i>p</i>	
	NaOCH ₃		(Mixture of stereoisomers)	631
3,4-Methylenedioxyethyl n-Hexyl Ketone and		$\text{CH}_3\text{COCCHCO}_2\text{C}_2\text{H}_5$		
		$3,4\text{-CH}_2\text{O}_2\text{C}_6\text{H}_4\text{CHCH}_2\text{COC}_6\text{H}_4\text{H}_{13}$	<i>n</i>	
		(At 5°, 65%)		481
Ethyl acetate	NaOC ₂ H ₅		<i>n</i> -H ₁₃ C ₆	
		(At reflux 50%, together with some of the 6-carbethoxy derivative)		632, 633

Note. References 432-433 are on pp. 545-555.

TABLE III—Continued

MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC KETONES			References
Reactants	Catalyst	Product (Yield, %)	
<i>trans</i> -Dibenzoylethylene and		$A = C_6H_5COCH_2CH(COC_6H_5)$	
Diethyl benzylmalonate	$NaOC_2H_5$	$C_6H_5CH_2C(A)(CO_2C_2H_5)_2$ (20)	58
Acetophenone	$NaOCH_3$	1,2,3-Tribenzylpropane (1)	634
1,2-Dibenzoyl ethane	$NaOC_6H_5$	$C_6H_5COCH_2CH(A)COC_6H_5$ (92)	634
1,1-Dibenzoyl ethane (Enol) and			
Cyanoacetamide	$(C_2H_5)_2NH$	3-Cyano-5-methyl-4,6-diphenyl-2-pyridone	592
3,4-Diphenyl-3-buten-2-one and			
Phenylnitromethane	$(C_2H_5)_2NH$	1-Nitro-1,2,3-triphenylpentan-4-one (68)	29
2-Benzoyl-1-phenylpropene and			
Dimethyl malonate	$NaOCH_3$	$C_6H_5COCH(CH_3)CH(C_6H_5)CH(CO_2CH_3)_2$ (two isomers: 52 ÷ 10)	76
2-Methoxy-1,3-diphenyl-2-propen-1-one and			
Cyanoacetamide	$NaOCH_3$	3-Cyano-5-methoxy-4,6-diphenyl-2-pyridone	631
Benzoyl- <i>p</i> -tolylmethane (Enol) and			
Cyanoacetamide	$(C_2H_5)_2NH$	3-Cyano-4-phenyl-6- <i>p</i> -tolyl-2-pyridone (34) and 3-cyano-6-phenyl-4- <i>p</i> -tolyl-2-pyridone (17)	370

2-Benzylidenemindan-1,3-dione and

Deoxybenzoin	NaOC_2H_5		416
<i>Styryl Phenethyl Ketone and</i>			
Dimethyl malonate	NaOCH_3	$A = \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{COCH}_2\text{CHC}_6\text{H}_5$	423
Diethyl malonate	NaOC_2H_5	$\text{A} = \text{CH}(\text{CO}_2\text{CH}_3)_2$	198
3-Benzoyl-4-phenyl-3-buten-2-one and		4-Carboethoxy-2-benzyl-5-phenylcyclohexane-1,3-dione (60)	
Phenylnitromethane	$(\text{C}_2\text{H}_5)_3\text{NIH}$		
$p\text{-CH}_3\text{C}_6\text{H}_4\text{COCH}_2\text{C}(=\text{NH})\text{CH}_3$	None		
3-Methoxy-3-phenyl-1-p-tolyl-2-propen-1-one and		3-Benzoyl-5 nitro-4,5 diphenylpentan-2-one (38)	29
Cyanoacetamide	$(\text{C}_2\text{H}_5)_3\text{NIH}$	5-Acetyl-2-methyl-4,6-diphenyl-3-p-toluoyl-3,4-dihydropyridine	398
3-Methoxy-1-phenyl-3-p-anisyl-2-propen-1-one and		3-Cyano-4-phenyl-6-p-tolyl-2-pyridone	370
Cyanoacetamide	$(\text{C}_2\text{H}_5)_3\text{NIH}$	3 Cyano 4-p-anisyl-6-phenyl-2-pyridone	594
Fluorenylideneacetophenone [†] and			
Acetophenone	KOH , acetal	9,9-Diphenacylfluorene	635
5-Mesitylacenaphthylene and			
Diethyl malonate	NaOC_2H_5	5-Mesitylacenaphthene-1-acetic acid** (50)	636

Note: References 491-1045 are on pp. 545-555.

[†] The unsaturated ketone was formed *in situ* from fluorenone and acetophenone.

** The acid was obtained after hydrolysis of the adduct

TABLE IV

MICHAEL CONDENSATIONS WITH ETHYLENIC KETONES OF THE DIBENZYLIDENE- AND DICINNAMYLIDENE-ACETONE TYPE

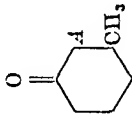
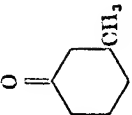
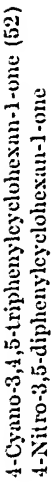
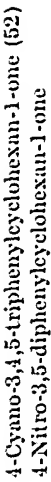


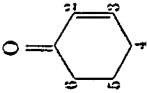
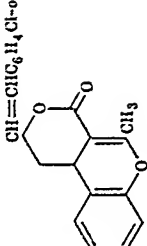
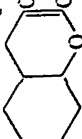
Reactants	Catalyst	Product (Yield, %)	References
<i>Dibenzylidenecetone and</i>			
$A = C_6H_5CH=CHCOCH_2CHC_6H_5$			
Dimethyl malonate	Piperidine $NaOCH_3$	$ACH(CO_2CH_3)_2$ (59)	198
Diethyl malonate	Piperidine $NaOCH_3$	Dimethyl 2,6-diphenyl-4-oxocyclohexane-1,1-dicarboxylate	198
Ethyl acetate	$(C_2H_5)_2NH$ $NaOCH_3$	$ACH(CO_2C_2H_5)_2$	198
Methyl cyanoacetate	$NaOH$	Diethyl 2,6-diphenyl-4-oxocyclohexane-1,1-dicarboxylate	21
Ethyl cyanoacetate	$NaOC_2H_5$	$CH_3COCH(A)CO_2C_2H_5$ (38)	198, 199
		4-Carbomethoxy-4-cyano-3,5-diphenylcyclohexan-1-one (72)	199
		4-Carbomethoxy-4-cyano-3,5-diphenylcyclohexan-1-one	200
		4-Carbomethoxy-4-cyano-3,5-diphenylcyclohexan-1-one (88)	
3-Methylcyclohexanone	$(C_2H_5)_2NH$	<div style="display: flex; align-items: center; justify-content: center;"> <div style="text-align: center;">  </div> <div style="margin: 0 10px;">or</div> <div style="text-align: center;">  </div> </div>	616
Benzyl cyanide	$NaOCH_3$	γ -Cinnamoyl- α,β -diphenylbutyronitrile (two isomers), and 4-cyano-3,4,5-triphenylcyclohexan-1-one (total 44)	952
Nitromethane	$NaOCH_3$	<div style="display: flex; align-items: center; justify-content: center;"> <div style="text-align: center;">  </div> <div style="margin: 0 10px;">or</div> <div style="text-align: center;">  </div> </div>	198

TABLE IV—Continued

MICHAEL CONDENSATIONS WITH ETHYLENIC KEYTONES OF THE DIBENZYLIDENE- AND DICINNAMYLIDENE-ACETONE TYPE
Substituted Dibenzylidenacetones—Continued


Substituent(s) in	Addend	Catalyst	Substituents in Product (Yield, %)	References
				
2-HO, 2'-Cl	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	NaOH, aq. ethanol	3-o-ClC ₆ H ₄ CH=CH—, 5-o-HOC ₆ H ₄ —, 6-C ₂ H ₅ O ₂ C— (28)	203
				203
	C ₆ H ₅ COCH ₂ CO ₂ C ₂ H ₅	NaOC ₂ H ₅		203

2-HO, 3'-Cl		$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$, NaOH, aq. ethanol	3- <i>m</i> -ClC ₆ H ₄ CH=CH—, 5- <i>o</i> -HOC ₆ H ₄ —, 6-C ₂ H ₅ O ₂ C— (3)	203
2-HO, 4'-Cl		$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$, NaOH, aq. ethanol	3- <i>p</i> -ClC ₆ H ₄ CH=CH—, 5- <i>o</i> -HOC ₆ H ₄ —, 6-C ₂ H ₅ O ₂ C— (33)	203
3-Cl, 4'-HO		$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$, NaOH, aq. ethanol	3- <i>m</i> -ClC ₆ H ₄ CH=CH—, 5- <i>p</i> -HOC ₆ H ₄ —, 6-C ₂ H ₅ O ₂ C— (85)	204
4-Cl, 4'-HO		$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$, NaOH, aq. ethanol	3- <i>p</i> -ClC ₆ H ₄ CH=CH—, 5- <i>p</i> -HOC ₆ H ₄ —, 6-C ₂ H ₅ O ₂ C— (70)	204
3-Cl, 4'-CH3O		$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$, NaOH, aq. ethanol	3- <i>p</i> -ClC ₆ H ₄ CH=CH—, 5- <i>m</i> -ClC ₆ H ₄ —, 6-C ₂ H ₅ O ₂ C— (55)	204
4-Cl, 4'-CH3O		$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$, NaOH, aq. ethanol	3- <i>p</i> -ClC ₆ H ₄ CH=CH—, 6- <i>p</i> -ClC ₆ H ₄ —, 6-C ₂ H ₅ O ₂ C— (45)	204

TABLE IV—Continued

MICHAEL CONDENSATIONS WITH ETHYLENIC KETONES OF THE DIENZYLDENE- AND DICINNAMYLIDENE-ACETONE TYPE

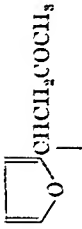

Substituted Dibenzylidenacetones—Continued

Substituent(s) in	Addend	Catalyst	Substituents in Product (Yield, %)	References
				
2,3'-Di-1H	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	NaOH, aq. ethanol	3- <i>o</i> -HOC ₆ H ₄ CH=CH—, 5- <i>o</i> -HOC ₆ H ₄ — (24)	202, 580
2-HO, 2'-CH ₃ O	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	NaOH, aq. ethanol	3- <i>o</i> -CH ₃ OC ₆ H ₄ CH=CH—, 5- <i>o</i> -HOC ₆ H ₄ —	202
2,2'-Di-CH ₃ O	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	NaOH, aq. ethanol	3- <i>o</i> -CH ₃ OC ₆ H ₄ CH=CH—, (88)	202
	CH ₃ COCH ₂ COCH ₃	NaOH, aq. ethanol	3- <i>o</i> -CH ₃ OC ₆ H ₄ CH=CH—	202
4,4'-Di-CH ₃	CH ₃ (CO ₂ CH ₃) ₂	NaOCH ₃	5- <i>o</i> -CH ₃ OC ₆ H ₄ —, 2-CH ₃ CO— 4,4-Dicarbomethoxy-3,5-di- <i>p</i> -methoxy- phenylcyclohexan-1-one	198
	NCCl ₃ CO ₂ CH ₃	NaOCH ₃	3,5-Di-(<i>p</i> -methoxyphenyl)-4-carbo- methoxy-1-cyanocyclohexan-1-one	199
4,4'-Di-(CH ₃) ₂ N	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	NaOH, aq. ethanol	3- <i>p</i> -(CH ₃) ₂ NC ₆ H ₄ CH=CH—, 5- <i>p</i> -(CH ₃) ₂ NC ₆ H ₄ —, 6-C ₂ H ₅ O ₂ C—	205
2-HO, 4'-(CH ₃) ₂ N	CH ₃ COCH ₂ CO ₂ C ₂ H ₅	KOH, aq. ethanol	3- <i>o</i> -HOC ₆ H ₄ CH=CH—, 5- <i>p</i> -(CH ₃) ₂ NC ₆ H ₄ —, 6-C ₂ H ₅ O ₂ C—	205
	NCCl ₃ CO ₂ C ₂ H ₅	NaOH, aq. ethanol	<i>p</i> -(CH ₃) ₂ NC ₆ H ₄ CH=CHCOCH ₃ — CH(C ₂ H ₅ OH- <i>o</i>)CH(CO ₂ H) ₂ *	205

Reactants	Catalyst	Product (Yield, %)	References
$2\text{-CH}_3\text{O}, 4'\text{-(CH}_3)_2\text{N}$	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$, NaOH, aq. ethanol	$3\text{-o-CH}_3\text{OC}_6\text{H}_4\text{CH=CH-}$, $5\text{-p-(CH}_3)_2\text{NC}_6\text{H}_4\text{-}$, $6\text{-C}_2\text{H}_5\text{O}_2\text{C-}$	205
$2\text{-HO}, 3\text{-CH}_3\text{O}, 4'\text{-(CH}_3)_2\text{N}$	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$, NaOH, aq. ethanol	$3\text{-(2-HO-3-CH}_3\text{OC}_6\text{H}_4)\text{CH=CH-}$, $5\text{-p-(CH}_3)_2\text{NC}_6\text{H}_4\text{-}$, $6\text{-C}_2\text{H}_5\text{O}_2\text{C-}$	205
$2\text{-HO}, 4\text{-CH}_3\text{O}, 4'\text{-(CH}_3)_2\text{N}$	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$, NaOH, aq. ethanol	$3\text{-p-(CH}_3)_2\text{NC}_6\text{H}_4\text{CH=CH-}$, $5\text{-(2-HO-4-CH}_3\text{OC}_6\text{H}_4)\text{-}$, $6\text{-C}_2\text{H}_5\text{O}_2\text{C-}$	205
$2\text{-HO}, 5\text{-CH}_3\text{O}, 4'\text{-(CH}_3)_2\text{N}$	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$, NaOH, aq. ethanol	$3\text{-(2-HO-5-CH}_3\text{OC}_6\text{H}_4)\text{CH=CH-}$, $5\text{-p-(CH}_3)_2\text{NC}_6\text{H}_4\text{-}$, $6\text{-C}_2\text{H}_5\text{O}_2\text{C-}$	205
$2\text{-OCH}_3, 4'\text{-Cl}$	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$, NaOCH ₃	$3\text{-p-CH}_3\text{OC}_6\text{H}_4\text{CH=CH-}$, $5\text{-o-CH}_3\text{OC}_6\text{H}_4\text{-}$, $6\text{-C}_2\text{H}_5\text{O}_2\text{C-}$ (57)	203
<i>Benzylidenecinnamylidenecedone and Dimethyl malonate</i>	NaOCH_3	4,4-Dicarbomethoxy-3-phenyl-5-styrylcyclohexan-1-one	198
<i>p-Methoxybenzylidenecinnamylidenecedone and Dimethyl malonate</i>	NaOCH_3	4,4-Dicarbomethoxy-3-p-methoxyphenyl-5-styrylcyclohexan-1-one	198
<i>Dacinnamylidenecedone and Dimethyl malonate</i>	NaOCH_3	4,4-Dicarbomethoxy-3,5-disstyrylcyclohexan-1-one	198
<i>2,6-Dibenzylidenecyclohexanone and Cyanacetamide</i>	NaOC_2H_5	Compound $\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}_2$	224

* The acid was obtained after hydrolysis of the adduct.

TABLE V
MICHAEL CONDENSATIONS WITH UNSATURATED KETONES CONTAINING HETEROCYCLIC RINGS

Reactants	Catalyst	Product (Yield, %)	References
<i>Furfurylideneacetone and</i>			
Benzyl cyanide 1-Nitropropane 2-Nitropropane Triethyl phosphonoacetate		$A = $ 	
	NaOCH ₃	C ₆ H ₅ CH(A)CN (81)	121
	(C ₂ H ₅) ₃ NH	CH ₃ CH ₂ CH(A)NO ₂ (75)	200
	(C ₂ H ₅) ₃ NH	(CH ₃) ₂ C(A)NO ₂ (95)	200
	NaOC ₂ H ₅	(C ₂ H ₅ O) ₃ P(O)CH(A)CO ₂ C ₂ H ₅ (9)	124
<i>Furfurylideneacetophenone and</i>			
Diethyl malonate Acetophenone Nitromethane 1-Nitropropane 2-Nitropropane Phenylnitromethane		$A = $ 	
	NaOC ₂ H ₅	ACH(CO ₂ C ₂ H ₅) ₂ (75)	210
	NaOC ₂ H ₅	C ₆ H ₅ COCH ₂ A (25)	207
	NaOCH ₃	ACH ₂ NO ₂	208
	(C ₂ H ₅) ₃ NH	CH ₃ CH ₂ CH(A)NO ₂ (70)	209
	(C ₂ H ₅) ₃ NH	(CH ₃) ₂ C(A)NO ₂ (90)	209
	NaOCH ₃	C ₆ H ₅ CH(A)NO ₂	208

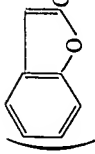
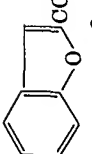
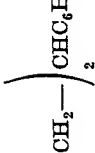

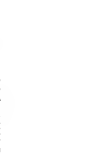


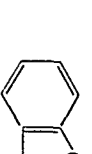
Furfurylideneacetophenones Containing a Substituent in the Phenyl Group

Substituent in	Adduct	Catalyst	Product (Yield, %)	References
4-Br	CH ₃ NO ₂	NaOCH ₃	 A =	208
4-CH ₃ O	C ₂ H ₅ CH ₂ NO ₂	NaOCH ₃	ACH ₃ NO ₂ , R = 4 Br (75)	208
4-Cyclohexyl	CH ₃ (CO ₂ C ₆ H ₁₁) ₂	NaOCH ₃	C ₆ H ₅ CH(A)NO ₂ , R = 4-Br (29)	210
	CH ₃ (CO ₂ CH ₃) ₂	NaOCH ₃	ACH ₃ (CO ₂ H) ₂ ,* R = 4-CH ₃ O	210
	CH ₃ (CO ₂ CH ₃) ₂	NaOCH ₃	ACH ₃ (CO ₂ CH ₃) ₂ , R = 4-cyclohexyl (50)	210

Reactants	Catalyst	Product (Yield, %)	References
2-Furfurydene-1-tetralone and			
Ethyl acetoacetate	NaOC ₂ H ₅		393
2-Furfurydene-6-methoxy-1-tetralone and			
Ethyl acetoacetate	NaOC ₂ H ₅		393

* The malonic ester adduct could not be obtained crystalline so it was hydrolyzed to the acid

TABLE V—Continued
MICHAEL CONDENSATIONS WITH UNSATURATED KETONES CONTAINING HETEROCYCLIC RINGS



Reactants	Catalyst	Product (Yield, %)	References
<i>Benzylidene-2-acetylcoumarone and</i> 2-Acetylcoumarone†	Aq. NaOH	 $\left(\text{COCH}_2 - \right)_2 \text{CHC}_6\text{H}_5$ and 	637
<i>Hydroxymethylene-2-acetylthiophene and</i> Diethyl acetone-1,3-dicarboxylate	NaOC_2H_5	 and 	427
<i>Hydroxymethylene-2-acetylpyridine and</i> Diethyl acetone-1,3-dicarboxylate	NaOC_2H_5	 and 	427
<i>Phenyl β-(4-Quinolyl)vinyl Ketone and</i> Acetophenone‡	NaOH	 and 	638

Note: References 491–1045 are on pp. 545–555.

† A mixture of benzaldehyde and 2-acetylcoumarone was used.

‡ A mixture of acetophenone and quinoline-4-carboxaldehyde was used.

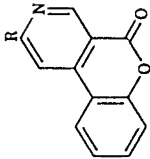
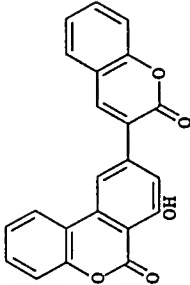
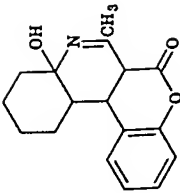
TABLE VI
MICHAEL CONDENSATIONS WITH 3-ACYLCOUMARINS AND RELATED COMPOUNDS*

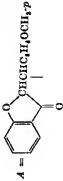

Reactants	Catalyst	Product (Yield, %)	References
3-Acetylcoumarin and			
		 unless complete structure is shown R = 3-Coumarinyl (45-52)*	211
Cyanoacetamide	None		
Acetone	Piperidine		212
Methyl ethyl ketone	$\text{NH}_2(\text{NCOCH}_2\text{CONH}_2)^\dagger$	R = CH_3 (32)	211
Acetophenone	$\text{NH}_2(\text{NCCCH}_2\text{CONH}_2)^\dagger$	R = C_6H_5 (42)	211
3-Acetylcoumarin	$\text{NH}_2(\text{NCOCH}_2\text{CONH}_2)^\dagger$	R = C_6H_5 (21)	211
	$\text{NH}_2(\text{NCCCH}_2\text{CONH}_2)^\dagger$	R = 3-Coumarinyl	212

* The cyanoacetamide could be replaced by malonamide, formamide, or urea without changing the product. The same product was obtained when piperidine was used as a catalyst. The earlier report (ref. 213) that the product with cyanoacetamide and piperidine was 3-acetyldihydrocoumarin-4-(α -cyanoacetamide) could not be confirmed.

† In these experiments cyanoacetamide was present; its decomposition furnished the ammonia.

TABLE VI—Continued
MICHAEL CONDENSATIONS WITH 3-ACYLCUMARINS AND RELATED COMPOUNDS

Reactants	Catalyst	Product (Yield, %)	References
3-Acetylcoumarin (Cont.) and		 <p>unless complete structure is shown</p>	
3-Acetylcoumarin	Piperidine	 <p>(18)</p>	
Cyclohexanone	$\text{NH}_3(\text{NCCCH}_2\text{CONH}_2)^\dagger$	 <p>(47)</p>	211

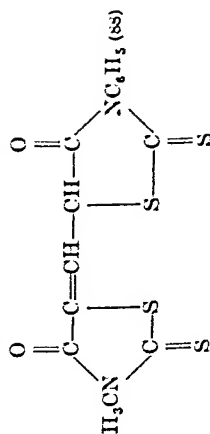
3-Benzylcoumarin and Cyanacetamide	Piperidine	3-Benzoyldihydrocoumarin-4-(α -cyanoacetamide)	213
7-Hydroxycoumarin and Cyanacetamide	Piperidine	7-Hydroxydihydrocoumarin-4-(α -cyanoacetamide) (90)	639
7-Methoxycoumarin and Cyanacetamide	Piperidine	7-Methoxydihydrocoumarin-4-(α -cyanoacetamide) (90)	639
2-(<i>p</i> -Methoxybenzylidene)coumaran 2-one† and		 $A = \text{CHCH}(\text{C}_6\text{H}_4\text{OCH}_3)_2$	
Ethyl acetoacetate Deoxybenzoin	NaOC ₂ H ₅ NaOC ₂ H ₅	$\begin{array}{l} \text{CH}_3\text{COCH}(A)\text{CO}_2\text{C}_2\text{H}_5 \\ \text{C}_6\text{H}_5\text{COCH}(A)\text{C}_6\text{H}_5 \end{array}$ 	214 214
Cyclohexanone	NaOC ₂ H ₅		214

Note: References 491-1045 are on pp. 545-555.

† In these experiments cyanoacetamide was present; its decomposition furnished the ammonia.
‡ The corresponding 6-methoxy compound behaves analogously with ethyl acetoacetate, deoxybenzoin, and cyclohexanone; ref. 214a.

TABLE VI—*Continued*
MICHAEL CONDENSATIONS WITH 3-ACYLCOUMARINS AND RELATED COMPOUNDS

Reactants	Catalyst	Product (Yield, %)	References
<i>γ</i> -Pyrone and Diethyl malonate	NaOC ₂ H ₅	Ethyl <i>p</i> -hydroxybenzoate	215
<i>Alkylidenrhodanines and</i> Rhodanine§	NH ₄ OH, NH ₄ Cl	α,α-Bis-(2-thio-4-ketotetrahydro-5-thiazolyl)ethane and homologs (22-55)	210
5-Ethoxymethylene-3-methylrhodanine and 3-Methylrhodanine	<i>t</i> -Amines	5,5'-Methyldynenebis-(3-methylrhodanine) (34-69)	640



(C₂H₅)₃N

3-Phenylrhodanine

640

3-Methylrhodanine

 $(C_5H_4N)_2$

640

3,3'-Ethylenebis-(5-thiazomethylenerhodanine) and
3-Methylrhodanine $(C_5H_4N)_2$

3-Phenylrhodanine

 $(C_6H_5)_2N$

640

Pyrazol blue and

1-Phenyl-3-methyl-2-pyrazolin-5-one

None

1-(p-Bromophenyl)-3-methyl-2-pyrazolin-5-one

None

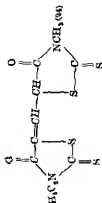
641

Pyrazolin-6-one

641

Note: References 491-1015 are on pp. 545-553.

‡ The actual ingredients used were rhodanine and various aliphatic aldehydes.



salt of 3,3'-ethylenebis-5-(2'-thiono-4'-keto-3'-methyl-5'-thiazolidymethylenerhodanine) (50)

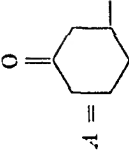
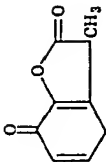
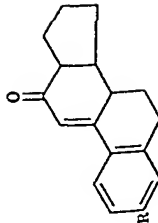
salt of 3,3'-ethylenebis 5-(2'-thiono-4'-keto-3'-phenyl-5'-thiazolidymethylenerhodanine) (37)



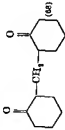
1,1',1''-Triphenyl-3,3',3''-trimethyl-(4,4',4''-ter-2-pyrazoline)-5,5',5''-trione

1,1'-Diphenyl-1''-(p-bromophenyl)-3,3',3''-trimethyl-(4,4',4''-ter-2-pyrazoline)-5,5',5''-trione

TABLE VII

MICHAEL CONDENSATIONS WITH CYCLOALKENONES AND ACYL CYCLOALKENES

Reactants	Catalyst	Product (Yield, %)	References
2-Hydroxymethylcyclopentanone and Ethyl acetacetate Diethyl acetone-1,3-dicarboxylate Ethyl β -aminocrotonate	NaOC_2H_5 NaOC_2H_5 —	5-Indanol-6-carboxylic acid (18) Diethyl 5-indanol-4,6-dicarboxylate (92) 6-Methyl-2,3-dihydro- β -pyridindene*	427 427 445
2-Cyclohexen-1-one and		 $A =$	
Diethyl malonate Nitromethane Nitroethane	NaOC_2H_5 NaOCH_3 NaOCH_3	$A\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (90) $A\text{CH}_2\text{NO}_2$ (50) $\text{CH}_3\text{CH}(A)\text{NO}_2$ (57)	642 643 643
3-Chloro-2-cyclohexen-1-one and			
Dimethyl methylmalonate	NaOCH_3		436
1-Acetyl-1-cyclopentene and			

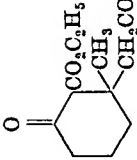
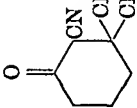
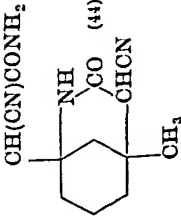
1-Tetralone	NaNH_2	$\text{R} = \text{H}$	98, 217
6-Methoxy-1-tetralone	NaNH_2	$\text{R} = \text{CH}_3\text{O}$ (55)	206
6-Ethoxy-1-tetralone	NaNH_2	$\text{R} = \text{C}_2\text{H}_5\text{O}$	217
Cycloheptanone	KOC_4H_9		614
2-Methylenecyclohexanone† and Ethyl acetoacetate	NaOH	2-Oxo-2,3,4,5,6,7,8,10-octahydronaphthalene	528
Methyl ethyl ketone	$\text{KOH}, \text{CH}_3\text{OH}$		645
Cyclohexanone	$\text{KOH}, \text{CH}_3\text{OH}$		645, 646‡

Note: References 491-1045 are on pp 545-555.

* This product was obtained after hydrolysis and decarboxylation.
 † 2-Hydroxymethylcyclohexanone was used in these experiments.
 ‡ A mixture of cyclohexanone and formaldehyde was employed.

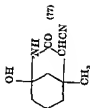
TABLE VII—Continued

MICHAEL CONDENSATIONS WITH CYCLOALKENONES AND ACYL CYCLOALKENES

Reactants	Catalyst	Product (Yield, %)	References
3-Methyl-2-cyclohexen-1-one and Diethyl malonate	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OCH}_3$	 (50)	62, 647, cf. 69, 175
Ethyl acetoacetate	NaOC_2H_5	1-Methylbicyclo[3.3.1]nonan-5-ol-7-one	648, 69
Ethyl cyanoacetate	NaOC_2H_5	 (13-21)	62, 647, cf. 18, 70
Ethyl cyanoacetate	NH_3	 (44)	649

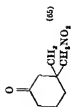
Cyanosuccinimide

Piperidine



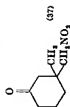
649

Nitromethane

 $(C_6H_5CH_2N(CH_3)_3)OCH_3$


652

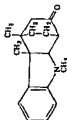
Hyperidine, 1/15 mole



650

1,3-Dimethylindole

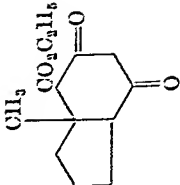
HCl



651

Note: References 491-1015 are on pp. 515-556.

TABLE VII—Continued
MICHAEL CONDENSATIONS WITH CYCLOALKENONES AND ACYL CYCLOALKENES

Reactants	Catalyst	Product (Yield, %)	References
<i>2-Hydroxymethylcyclohexanone and</i>			
Ethyl acetate	NaOC_2H_5	Ethyl 6-hydroxytetralin-7-carboxylate (50)	427
Diethyl acetone-1,3-dicarboxylate	NaOC_2H_5	Diethyl 6-hydroxytetralin-5,7-dicarboxylate (83)	427
Cyanoacetamide	Piperidine; $(\text{C}_2\text{H}_5)_2\text{NH}$	3-Cyano-5,6,7,8-tetrahydroquinolin-2-ol	224
$\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	None	Ethyl 2-methyl-5,6,7,8-tetrahydroquinoline-3-carboxylates	443, 652
$\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CN}$	None	3-Cyano-2-methyl-5,6,7,8-tetrahydroquinoline	653
$\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{COCCH}_3$	None	3-Acetyl-2-methyl-5,6,7,8-tetrahydroquinoline	653
$\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{COC}_6\text{H}_5$	None	3-Benzoyl-2-methyl-5,6,7,8-tetrahydroquinoline	653
<i>2-Aminomethylcyclohexanone and</i>			
Ethyl cyanoacetate	Na	4-Cyano-3-oxo-2,3,5,6,7,8-hexahydroisoquinoline	446
<i>1-Acetyl-2-methyl-1-cyclopentene and</i>			
Diethyl malonate	NaOC_2H_5		424
Diethyl phenethylmalonate	NaOC_2H_5	Acid, $\text{C}_{10}\text{H}_{16}\text{O}_3$ (poor)	218

Cyclopentylidenecetone and

Diethyl malonate

 NaOC_2H_5 

221

1-Acetyl-1-cyclohexene and

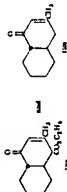
Diethyl malonate

 NaOC_2H_5

cis- and *trans*-6-Carboethoxydecalin-1,2-diolide
(7, 87, 60)

94, 95, 96,
654

Ethyl acetoacetate

 NaOC_2H_5 

93

Cyclohexanone

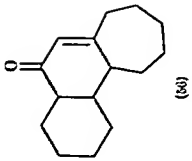
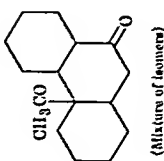
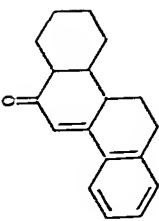
 NaNH_2 

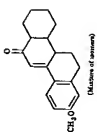
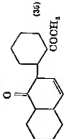
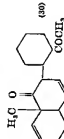
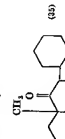
99, cf. 94

Note: References 491-1045 are on pp. 545-555.

§ At 0° the product is ethyl 9-hydroxy-2-methyl-5,6,7,8,9,10-hexahydroquinoline-3-carboxylate.

TABLE VII—Continued
MICHAEL CONDENSATIONS WITH CYCLOALKENONES AND ACYL CYCLOALKENES

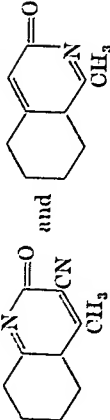
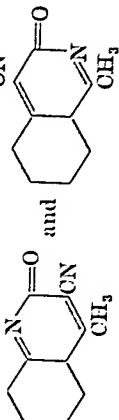

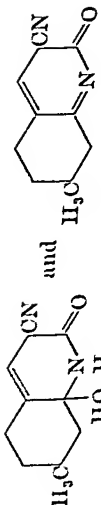
Reactants	Catalyst	Product (Yield, %)	References
1-Acetyl-1-cyclohexene (Cont.) and			
Cycloheptanone	$\text{KOC}_4\text{H}_9\text{-}l$	 (66)	644
1-Acetyl-1-cyclohexene	NaNH_2	 (Mixture of isomers)	97
1-Tetralone	NaNH_2		313

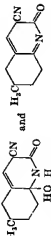
6-Methoxy-1-tetralone	NaNH ₂		98
cis-1-Decalone	NaNH ₂		855
1-Oxo-9-methyl-1,2,5,6,7,8,9,10-octahydronaphthalene	NaNH ₂		855
3,8-Dimethyl-4,7,8,9-tetrahydro-indan-1-one	NaNH ₂		655
2-Methoxymethylcyclohexan-1-one and Ethyl acetate	NaOCH ₂ H ₅		656

2-Hydroxy-5,6,7,8-tetrahydro-3-naphthoic acid and
ethyl α -acetyl- β -(2-ketocyclohexyl)acrylate

Note: References 491-1045 are on pp. 545-555.

TABLE VII—Continued

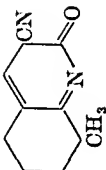
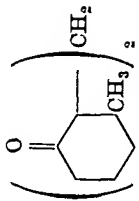
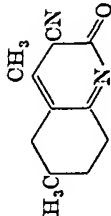
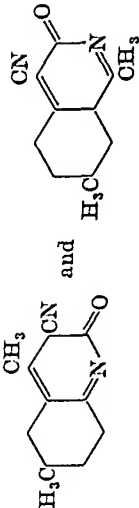
Reactants	Catalyst	Product (Yield, %)	References
2-(α -Hydroxyethylidene)cyclohexan-1-one and Diethyl acetone-1,3-dicarboxylate NaOC_2H_5		5,7-Dicarboethoxy-8-methyl-6-hydroxy- 1,2,3,4-tetrahydronaphthalene (36)	427
Cyanoacetamide	Piperidine; NaOC_2H_5		941
N-Methylcyanoacetamide	Piperidine; NaOC_2H_5		941
3,5-Dimethyl-2-cyclohexen-1-one and Ethyl acetate	NaOC_2H_5	1,3-Dimethyl-5-hydroxybicyclo[3.3.1]nonan-7-one	657
2-Hydroxymethylcyclohexanone and Ethyl cyanoacetate	$(\text{C}_2\text{H}_5)_2\text{NH}$		224
Cyanoacetamide	Piperidine; $(\text{C}_2\text{H}_5)_2\text{NH}$		224

2-Aminomethylene-3-methylcyclohexanone and Ethyl cyanoacetate	Na		5-Methyl-3-oxo-2,3,5,6,7,8-hexahydroisoquinoline- 4-carbonamide	446
2-Hydroxymethylene-4-methylcyclohexanone and Cyanoacetamide	sec-Amine			224
$\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	None		Ethyl 2,6-dimethyl-5,6,7,8-tetrahydroquinoline-3- carboxylate	443
$\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{COCH}_3$	None		3-Acetyl-2,6-dimethyl-5,6,7,8-tetrahydroquinoline	653
$\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{COC}_2\text{H}_5$	None		3-Benzoyl-2,6-dimethyl-5,6,7,8-tetrahydroquinoline	443
2-Aminomethylene-4-methylcyclohexanone and Ethyl cyanoacetate	Na		6-Methyl-3-oxo-2,3,5,6,7,8-hexahydroisoquinoline- 4-carbonitrile	446
2-Hydroxymethylene-5-methylcyclohexanone and $\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	None		Ethyl 2,7-dimethyl-5,6,7,8-tetrahydroquinoline 3- carboxylate	443
$\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{COCH}_3$	None		3-Acetyl-2,7-dimethyl-5,6,7,8-tetrahydroquinoline	653
$\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{COC}_2\text{H}_5$	None		3-Benzoyl-2,7-dimethyl-5,6,7,8-tetrahydroquinoline	653
2-Aminomethylene-5-methylcyclohexanone and Ethyl cyanoacetate	Na		7-Methyl-3-oxo-2,3,5,6,7,8-hexahydroisoquinoline- 4-carbonitrile	446

Note: References 491-1045 are on pp. 545-555.

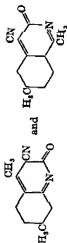
TABLE VII—Continued

MICHAEL CONDENSATIONS WITH CYCLOALKENONES AND ACYL CYCLOALKENES

Reactants	Catalyst	Product (Yield, %)	References
2-Hydroxymethylcyclohexanone and Cyanacetamide	<i>sec</i> -Amine		224
$\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	None	Ethyl 2,8-dimethyl-5,6,7,8-tetrahydroquinoline-3-carboxylate (42)	653
2-Methylcyclohexanone	KOH, $\text{C}_2\text{H}_5\text{OH}$		646
3-Methylcyclohexanone	Piperidine; NaOC_2H_5		941
2-(α -Hydroxyethylidene)-4-methylcyclohexan-1-one and Cyanacetamide	Piperidine; NaOC_2H_5		941

2-(α -Hydroxyethylidene)-5-methylcyclohexan-1-one and

Cyanoacetamide

Piperidine; NaOC_2H_5 

841

2-(α -Hydroxyethylidene)-8-methylcyclohexan-1-one and

Cyanoacetamide

Piperidine; NaOC_2H_5 

941

2-Hydroxymethylcyclohexanone and

Diethyl acetone-1,3-dicarboxylate NaOC_2H_5 $\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ None

Diethyl 3-hydroxybicyclo[5.4.0]undeca-1(6),2,4-triene-2,4-dicarboxylate (61)

428

Methyl α -Cyclopentylidenemethyl Ketone andDiethyl malonate NaOC_2H_5

Ethyl 6 methyl-2,3-dihydropyridene 7-carboxylate

652

3-Methylcyclopentylidenecetone and

Diethyl malonate

1-Methylspiro[5.4]decane-2,4-dione (low)

220

Cyclohexylidenecetone and

Diethyl malonate

8-Methylspiro[5.4]decane-2,4-dione

659


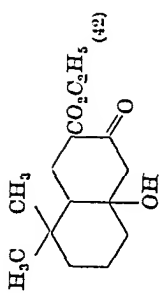
 NaOC_2H_5
 NaOCH_3 1-Carbethoxyspiro[5.5]undecane-2,4-dione (84)
Spiro[5.5]undecane-2,4-dione (70-80)

221, 390

654

Note: References 491-1045 are on pp. 545-555.

TABLE VII—Continued

MICHAEL CONDENSATIONS WITH CYCLOALKENONES AND ACYL CYCLOALKENES			References
Reactants	Catalyst	Product (Yield, %)	
2-Methylene-3,3-dimethylcyclohexanone and			
Ethyl acetoneacetate	NaOC_2H_5	  or	659
2-Hydroxymethylene-4,5-dimethylcyclohexanone and $\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	None	Ethyl 2,6,7-trimethyl-5,6,7,8-tetrahydroquinoline-3-carboxylate	653
Isophorone and Nitromethane	Piperidine	5-Nitromethyl-3,3,5-trimethylcyclohexanone (9)	650
1-Acetyl-2-methyl-1-cyclohexene and Diethyl malonate	NaOC_2H_5	10-Methyldecalin-1,3-dione (low) 4-Carbethoxy-10-methyldecalin-1,3-dione (good)	66 660

401, 384

 KOC_4H_9 , t

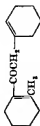
1-Acetyl-8-methyl 1 cyclohexene and

 KOC_4H_9 , t

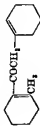
Cyclohexanone

401

Note: References 491-1045 are on pp. 545-555.
 || A 50% yield of

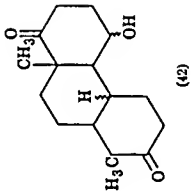
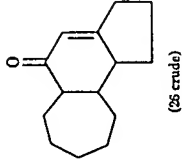
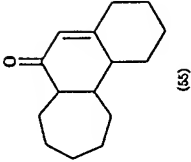



was also obtained. Other authors (ref. 387) describe this compound as the only product of the reaction
 ¶ In addition, a 46% yield of



was obtained.

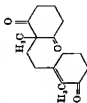
TABLE VII—continued
MICHAEL CONDENSATIONS WITH CYCLOALKENONES AND ACYL CYCLOALKENES

Reactants	Catalyst	Product (Yield, %)	References
2-Methyl-3-vinyl-2-cyclohexen-1-one and 2-Methylcyclohexanone-1,3-dione	$(C_2H_5)_2NH$	 (42)	661
1-Acetylcycloheptene and Cyclopentanone	$NaOCH_3$	 (25 crude)	644
Cyclohexanone	KOC_4H_9-l	 (55)	644

Cycloheptanone	KOC_4H_9		044
2-Hydroxymethylcyclooctanone and Diethyl acetone-1,3-dicarboxylate	NaOC_2H_5	(a)	428
3-Methyl 5-n-propyl-2-cyclohexen-1-one and Nitromethane	Piperidine	Diethyl 3-hydroxybicyclo[3.4.0]dodeca-1(6),2,4-triene-2,4-dicarboxylate (59)	650
2-Methylcyclohexylidenecetone and Diethyl malonate	NaOC_2H_5	3-Methyl-3-nitromethyl-5-n-propylcyclohexanone (25)	220

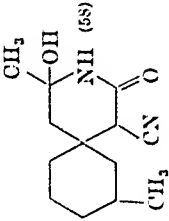
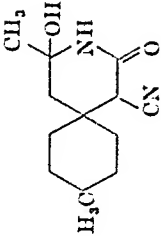
Note: References 491-1045 are on pp. 545-555.

•• This product is formed from an intermediate of the formula



which has, however, not been isolated.

TABLE VII—Continued
MICHAEL CONDENSATIONS WITH CYCLOALKENONES AND ACYL CYCLOALKENES

Reactants	Catalyst	Product (Yield, %)	References
3-Methylcyclohexylidenecacetone and Diethyl malonate	NaOC_2H_5	8-Methylspiro[5.5]hendecane-2,4-dione	220
Cyanoacetamide	NaOC_2H_5		602
4-Methylcyclohexylidenecacetone and Ethyl cyanoacetate	NaOC_2H_5	9-Methylspiro[5.5]hendecane-2,4-dione	220
Cyanoacetamide	NaOC_2H_5		602
Carrone and Ethyl acetate	NaOC_2H_5	5-Hydroxy-3-isopropenyl-9-methylbicyclo[3.3.1]nonan-7-one (54)	431
Ethyl cyanoacetate	$(\text{C}_2\text{H}_5)_2\text{NH}$	Ethyl 2-methyl-5-isopropenylcyclohexanone-3-cyanoacetate (25-33)	20

Umbellidone and

Diethyl malonate

 NaOC_2H_5

143



1-Acetyl-2,6-dimethylcyclohexene and

Diethyl malonate

 NaOC_2H_5 *trans*(?) 8,10-Dimethyldecalin-1,3-dione

4-Carboxy-8,10-dimethyldecalin-1,3-dione (42)

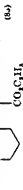
96

660, 90

1-Acetyl-6,8-dimethylcyclohexene and

Diethyl α-acetylacrylate

Na



663

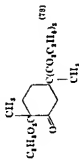
6-Carboxy 6-methyl-2-cyclohexen-1-one and

Diethyl malonate

 NaOC_2H_5 

664

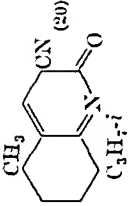
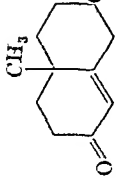
Diethyl methylmalonate

 NaOC_2H_5 

168

Note: References 491-1015 are on pp. 645-653

TABLE VII—Continued
MICHAEL CONDENSATIONS WITH CYCLOALKENONES AND ACYL CYCLOALKENES

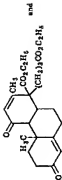
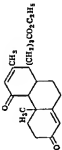
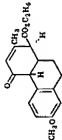
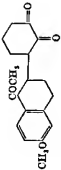
Reactants	Catalyst	Product (Yield, %)	References
1-Butyryl-2-methyl-1-cyclohexene and Diethyl malonate	NaOC_2H_5	<i>trans</i> (?) 2-Ethyl-10-methyldecalin-1,3-dione	96
2-Hydroxymethylcyclohexanone and Cyanoacetamide	<i>sec</i> -Amine	 (20)	224
2-Hydroxymethylcyclohexanone and Malonic acid Cyanoacetic acid	None None	β -Camphorylidene- β -propionic acid (50) β -Camphorylidene- β -propionitrile (80)	366 366
10-Methyl-2-oxo-2,3,4,5,6,10-hexahydronaphthalene and Diethyl malonate	NaOC_2H_5	 (33)	190
2-Hydroxymethylcyclohexanone and Diethyl acetone-1,3-dicarboxylate	NaOC_2H_5	Diethyl 3-hydroxybicyclo[5.4.0]tetradeca-1(6),2,4-triene-2,4-dicarboxylate (60)	428
2-Phenyl-2-cyclopenten-1-one and Diethyl malonate Dibenzyl malonate	NaOC_2H_5 KOC_4H_9 - <i>t</i>	Diethyl 2-phenylcyclopentan-1-one-3-malonate (47) 3-Oxo-2-phenylcyclopentanecarboxylic acid (53)††	685 606

1-Benzoylcyclopentene and Dibenzyl malonate	KOC_4H_9 , †	<i>trans</i> (?) 2-Benzoylcyclopentylmalonic acid	607
2-Phenyl-2-cyclohexen-1-one and Diethyl malonate	NaOC_2H_5	Diethyl <i>trans</i> 2-phenylcyclohexan-1-one-3-malonate (96)	105, 100, 608, 609
Dibenzyl malonate	KOC_4H_9 , †	Dibenzyl <i>trans</i> 2-phenylcyclohexan-1-one-3-malonate (90)	108, 608
Methyl cyanoacetate	NaOCH_3	Methyl 2-phenylcyclohexan-1-one-3-cyanoacetate (80)	100, 608
Benzyl cyanoacetate	KOC_4H_9 , †	<i>trans</i> 3-Cyanomethyl-2-phenylcyclohexan-1-one (86)	108
Nitromethane	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OCH}_3$	2-Phenyl-3-nitromethylcyclohexan-1-one (80)	106, 608
Methyl nitroacetate	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OCH}_3$	Methyl <i>trans</i> -2-phenylcyclohexan-1-one-3-nitroacetate (90)	100, 608
6-Phenyl-2-cyclohexen-1-one and Dibenzyl malonate ††	KOC_4H_9 , †	<i>trans</i> -6-Phenylcyclohexanone-3-acetic acid ††	107
4-Phenyl-2-cyclohexen-1-one and Dibenzyl malonate ††	KOC_4H_9 , †	<i>trans</i> -4-Phenylcyclohexanone-3-acetic acid ††	107
Cyclohexylidenecyclohexanone and Cyanoacetamide	NaOC_2H_5	Compound $\text{C}_{13}\text{H}_{16}\text{N}_2\text{O}$	670
1-Bulargyl-2,6-dimethylcyclohexene and Diethyl malonate	NaOC_2H_5	<i>trans</i> (?) 2-Ethyl-8,10 dimethyldecaln-1,3-dione	96

Nde. References 491-1045 are on pp. 545-555.

†† A mixture of 4- and 6 phenyl-2-cyclohexen-1-one was used in this experiment.

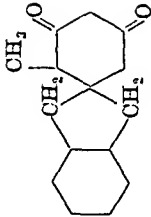
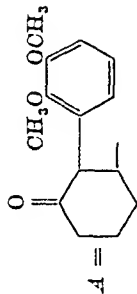
‡‡ The product was obtained after hydrolysis and partial decarboxylation.

1-Benzocyclohexene and Dibenzyl malonate	KOC_2H_5 , <i>t</i>	<i>trans</i> (?) 2-Benzoylcyclohexylmalonic acid (84)	607
2-Phenyl-2-cyclohepten-1-one and Dibenzyl malonate	KOC_2H_5 , 4	Dibenzyl 2-phenylcycloheptan-1-one-3-malonate (90)	108
1-Acetyl-9-methyl-6-oxo-3,4,0,7,8,9-hexahydronaphthalene and			603
Diethyl α-acetyladipate	Na		
1-Acetyl-6-methoxy-3,4-dihydronaphthalene and			673
Ethyl acetoacetate	NaOC_2H_5		674
Cyclohexane-1,2-dione	—		

Note: References 491-1045 are on pp. 545-555

‡‡ The product was obtained after hydrolysis and partial decarboxylation.

TABLE VII—Continued

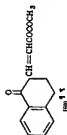
MICHAEL CONDENSATIONS WITH CYCLOALKENONES AND ACYL CYCLOALKENES				References
Reactants	Catalyst	Product (Yield, %)		
<i>Methyl α-Hydrindanylideneethyl Ketone and</i>				
Diethyl malonate	Na		223	
<i>2-Hydroxymethylencyclohexanone and</i>				
Diethyl acetone-1,3-dicarboxylate	NaOC ₂ H ₅	Diethyl 3-hydroxybicyclo[10.4.0]-1(6),2,4-triene-2,4-dicarboxylate	428	
<i>2-(2',3'-Dimethoxyphenyl)-2-cyclohexen-1-one and</i>				
				
Dimethyl malonate	NaOCH ₃	ACH(CO ₂ CH ₃) ₂ (97)	106, 608	
Diethyl malonate	NaOC ₂ H ₅	ACH(CO ₂ C ₂ H ₅) ₂ (94)	106, 608	
Dibenzyl malonate	KOC ₄ H ₉ -t	ACH(CO ₂ CH ₂ C ₆ H ₅) ₂ (88)	108, 609	
Methyl cyanoacetate	NaOCH ₃	ACH(CN)CO ₂ CH ₃ (95)	106, 608	
Ethyl cyanoacetate	NaOC ₂ H ₅	ACH(CN)CO ₂ C ₂ H ₅ (90)	106, 608	
Benzyl cyanoacetate	KOC ₄ H ₉ -t	ACH ₂ CN (82)§§	108, 609	
Methyl nitroacetate	[C ₆ H ₅ CH ₂ N(CH ₃) ₂]OCH ₃	ACH(NO ₂)CO ₂ CH ₃ (90)	106, 608	
<i>1-Benzoylcycloheptene and</i>				
Dibenzyl malonate	KOC ₄ H ₉ -t	trans(?) - 2-Benzoylcycloheptylmalonic acid (48)	607	

2-Isopropoxymethylene-1-tetralone and

Diacetyl monodimethyl ketal

Na

675



and

(Lone)

2-(2',3',4'-Trimethoxyphenyl)-2-cyclohepten-1-one and
Diethyl malonateKOC₂H₅, t

676

3-Oxo-2-(2',3',4'-trimethoxyphenyl)cycloheptane-1-
acetic acid (72)††

Zeranolone



and

Ethyl cyanoacetate

Compound C₁₈H₁₈N₄O₄

677

Note: References 491-1045 are on pp. 545-655.

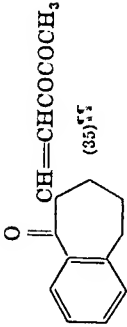
†† The product was obtained after hydrolysis and partial decarboxylation.

‡‡ This product was obtained after partial hydrolysis and decarboxylation.

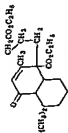
§§ The product was obtained after hydrolysis.

¶¶ This product results from spontaneous dehydrogenation or disproportionation of the expected compound.

TABLE VII—Continued
MICHAEL CONDENSATIONS WITH CYCLOALKENONES AND ACYL CYCLOALKENES

Reactants	Catalyst	Product (Yield, %)	References
<i>2-Isopropoxymethylcyclohexenylacetone and</i>			
Biacetyl monodimethyl ketal	Na	 (35) ⁵⁵	675
<i>2-Cyclopentadecen-1-one and</i>			
Diethyl malonate	NaOC ₂ H ₅	Diethyl cyclopentadecan-1-one-3-malonate (41)	532
<i>2-Hydroxymethylcyclopentadecanone and</i>			
Diethyl acetone-1,3-dicarboxylate	NaOC ₂ H ₅	Diethyl 3-hydroxybicyclo[13.4.0]nonadeca-1(8),2,4,triene-2,4-dicarboxylate (79)	428
<i>2-Hydroxymethylcyclohexadecanone and</i>			
Diethyl acetone-1,3-dicarboxylate	NaOC ₂ H ₅	Diethyl 3-hydroxybicyclo[14.4.0]eicosa-1(8),2,4,triene-2,4-dicarboxylate (35)	428

3,5-Cholestadien-7-one and
Diethyl malonate

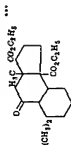


$\text{NaO}_2\text{C}_2\text{H}_5$: piperidine

Diethyl 7-oxo-5-cholestene-3-malonate (50)

678

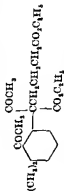
$\text{C}_4\text{H}_9\text{N}(\text{CH}_3)\text{MgBr}$



663

Note: References 491-1045 are on pp. 545-555

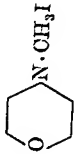

†† This product results from spontaneous dehydrogenation or disproportionation of the expected compound.
*** This reaction takes place when


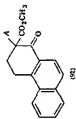


is treated with the reagent or when 1-acetyl 6,6-dimethyl-1-cyclohexene is condensed with ethyl α -acetylmalonate in the presence of sodium amide.

TABLE VIII

ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES

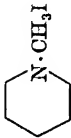
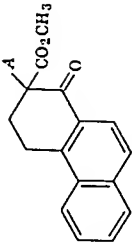
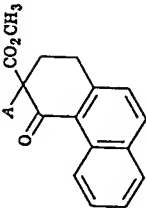
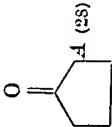
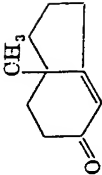
Substituent R in $\text{CH}_3\text{COCH}_2\text{CH}_2\text{R}$	Addend	Catalyst	Product (Yield, %) $A = \text{CH}_3\text{COCH}_2\text{CH}_2-$	References
$(\text{CH}_3)_2\text{N}$	$\text{CH}_2(\text{CO}_2\text{C}_2\text{H}_5)_2$	NaOC_2H_5	$A\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$	679
$(\text{C}_2\text{H}_5)_2\text{N} \cdot \text{CH}_3\text{I}$	$\text{C}_6\text{H}_5\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$	NaNH_2	$\text{C}_6\text{H}_5\text{C}(A)(\text{CO}_2\text{C}_2\text{H}_5)_2$	680
$(\text{CH}_3)_2\text{N}$	$\text{CH}_3\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5$	NaOC_2H_5	4-Carboethoxy-3-methyl-2-cyclohexen-1-one	629, 681
$(\text{CH}_3)_2\text{N} \cdot \text{CH}_3\text{I}$	$\text{CH}_3\text{COCH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$	—	3,6-Dimethyl-2-cyclohexen-1-one	682
$(\text{C}_2\text{H}_5)_2\text{N} \cdot \text{CH}_3\text{I}$	$\text{CH}_3\text{COCH}(\text{CH}_2\text{C}_6\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5$	—	6-Benzyl-3-methyl-2-cyclohexen-1-one	683
	Ethyl isobutyrylacetate	NaOC_2H_5	Ethyl 2-isobutyryl-5-oxohexanoate (65)	684
	Ethyl α -acetylisovalerate	NaOC_2H_5	6-Isopropyl-3-methyl-2-cyclohexen-1-one* (50)	100
$(\text{C}_2\text{H}_5)_2\text{N} \cdot \text{CH}_3\text{I}$	Diethyl α -methyloxalacetate	NaOC_2H_5	Ethyl 1-methyl-2,4-dioxocyclohexan-1-pyruvate	685
	Dimethyl α -methyl- β -oxoadipate	NaOCH_3 , pyridine		686
$(\text{C}_2\text{H}_5)_2\text{N}$	2-Carboethoxycyclohexan-1-one	NaOC_2H_5 , pyridine	$\text{CH}_3\text{CO}_2\text{CH}_2$ 2-(β -Acetyloethyl)-2-carboethoxycyclohexan-1-one	230

$(C_4H_9)_3N \cdot CH_2I$	2-Carbethoxycyclohexan-1-one	$NaOC_2H_5$		68, 229
	2-Carbomethoxycycloheptan-1-one	$NaOCH_3$	2-(β -Acetyllethyl)-2-carbomethoxycycloheptan-1-one (86)	688
	2-Carbomethoxycyclooctan-1-one	$NaOCH_3$	2-(β -Acetyllethyl)-2-carbomethoxycyclooctan-1-one (78)	689, 690
	2-Carbomethoxycyclononan-1-one	$NaOCH_3$	2-(β -Acetyllethyl)-2-carbomethoxycyclononan-1-one (80)	689, 690
	2-Carbomethoxycyclopentadecan-1-one	$NaOCH_3$	2-(β -Acetyllethyl)-2-carbomethoxycyclopentadecan-1-one (78)	688
	Methyl 1-oxo-1,2,3,4-tetrahydrophenanthrene-2-carboxylate	$NaOCH_3$		485

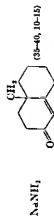
Note. References 491-1015 are on pp. 545-555.

• This product, piperitone, results from hydrolysis and decarboxylation.

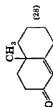
TABLE VIII—Continued
ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES

Substituent R in $\text{CH}_3\text{COCH}_2\text{CH}_2\text{R}$	Addend	Catalyst	Product (Yield, %) $A = \text{CH}_3\text{COCH}_2\text{CH}_2-$	References
	Methyl 1-oxo-1,2,3,4-tetrahydro- phenanthrene-2-carboxylate	NaOCH_3	 (35)	532
	Methyl 4-oxo-1,2,3,4-tetrahydro- phenanthrene-3-carboxylate	NaOCH_3	 (32)	533
$(\text{C}_2\text{H}_5)_2\text{N}$	CH_3COCH_3	None	3-Methyl-2-cyclohexen-1-one (10)	691
	Cyclopentanone	None	 (28)	691
$(\text{C}_2\text{H}_5)_2\text{N} \cdot \text{CH}_3\text{I}$	2-Methylcyclopentanone	NaNH_2 ; NaOC_2H_5	 (29)	229, 230

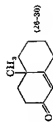
2-Methylcyclohexanone



229, 087



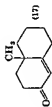
687



602

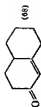


693



884, 190

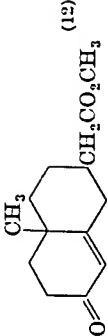
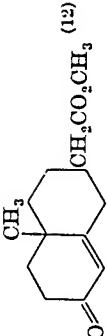
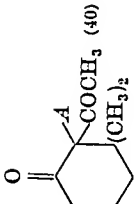
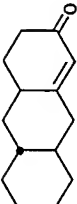
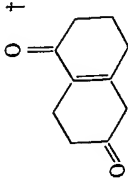
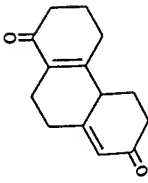
2-Formylcyclohexanone



694

Note. References 401-1015 are on pp 545-553.

TABLE VIII—Continued
ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES

Substituent R in $\text{CH}_3\text{COCH}_2\text{CH}_2\text{R}$	Addend	Catalyst	Product (Yield, %) $A = \text{CH}_3\text{COCH}_2\text{CH}_2-$	References
$(\text{C}_2\text{H}_5)_2\text{N} \cdot \text{CH}_3\text{I}$ (<i>Cont.</i>)	5-Carbomethoxymethyl-2-methyl- cyclohexan-1-one	NaOCH_3	 (12)	664
		NaNH_2	 (12)	664
2-Acetyl-3,3-dimethylcyclohexane- 1-one		NaOCH_3	 (40)	695
<i>trans</i> -2-Decalone		NaNH_2		229
 †		NaOCH_3		537

537

696

 NaOCH_3 

1-Methyl-2-decalone

 NaNH_2 

Note: References 191-1013 are on pp. 515-555

† The compound actually employed was the isomer of the structure







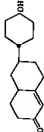
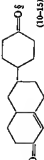
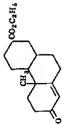

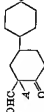
‡ A mixture of this compound with the isomer of the structure



was used. Part of the material was dehydrogenated to 6-hydroxy-5-methyl-1-tetralone.

TABLE VIII—Continued



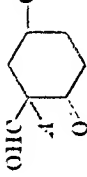
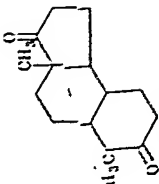
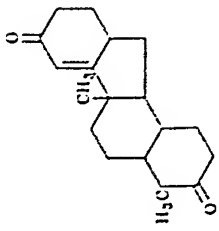
Substituent R in $\text{CH}_3\text{COCH}_2\text{CH}_2\text{R}$	Addend	Catalyst	Product (Yield, %) $A = \text{CH}_3\text{COCH}_2\text{CH}_2-$	References
$(\text{C}_2\text{H}_5)_2\text{N} \cdot \text{CH}_3\text{I}$ (Cont.)	4-Cyclohexyl-2-hydroxymethylene- cyclohexan-1-one	NaOCH_3	 (76) and (21)	700
	2-Hydroxymethylene-4-(<i>trans</i> -4'- hydroxycyclohexyl)cyclohexan- 1-one	NaOCH_3	 (35)§	532
$(\text{C}_2\text{H}_5)_2\text{N}$	2-Hydroxymethylene-4-(<i>trans</i> -4'- hydroxycyclohexyl)cyclohexan- 1-one	NaOCH_3	 (29)§	692
$(\text{C}_2\text{H}_5)_2\text{N} \cdot \text{CH}_3\text{I}$	2-Hydroxymethylene-4-(<i>cis</i> -4'-oxo- cyclohexyl)cyclohexan-1-one	NaOCH_3	 (40)§	532


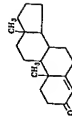




$(C_2H_5)_3N$	2-Hydroxymethylene-4-(cis-4'-oxo-cyclohexyl)cyclohexan-1-one	$NaOCH_3$		692
$(C_2H_5)_3N \cdot CH_3I$	2-Hydroxymethylene-4-(4'-oxo-cyclohexyl)cyclohexan-1-one	$NaOCH_3$		532, 602
	6-Carboethoxy-1-methyl 2-decalone	$NaNH_2$		697
	7,8-Dimethoxy-1-ethyl 2-tetralone	$NaNH_2$		701
$(CH_3)_3N \cdot I$	2-Hydroxymethylene-4-(4'-carboxy-cyclohexyl)cyclohexan-1-one	$NaOCH_3$		702

Note: References 491-1045 are on pp. 545-555

§ This product resulted from the cyclization of the primary product, which has not been isolated.

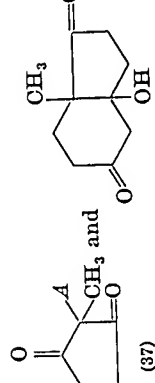
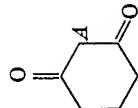
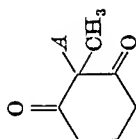
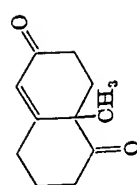
TABLE VIII—Continued
ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES






Substituent R in $\text{CH}_3\text{COCH}_2\text{CH}_2\text{R}$	Addend	Catalyst	Product (Yield, %) $A = \text{CH}_3\text{COCH}_2\text{CH}_2-$	References
$(\text{CH}_3)_2\text{N} \cdot \text{I}$ (<i>Cont.</i>)	2-Hydroxymethylene-4-(4'-carboxy-phenyl)cyclohexan-1-one	NaOCH_3	 $A = \text{CH}_3\text{COCH}_2\text{CH}_2-$ (51)	702
	2-Hydroxymethylene-4-(4'-carboxymethoxycyclohexyl)cyclohexan-1-one	NaOCH_3	 $A = \text{CH}_3\text{COCH}_2\text{CH}_2-$	702
	2-Hydroxymethylene-4-(4'-carboxymethoxyphenyl)cyclohexan-1-one	NaOCH_3	 $A = \text{CH}_3\text{COCH}_2\text{CH}_2-$ (51)	702
$(\text{C}_2\text{H}_5)_2\text{N} \cdot \text{CH}_3\text{I}$	 (Mixture of isomers)	NaNH_2	 $A = \text{CH}_3\text{COCH}_2\text{CH}_2-$	703

	NaNH_2		704
	<p>2-Hydroxymethylene-1-oxo-1,2,3,4-tetrahydrophenanthrene</p> <p>NaOCH_3</p>	 <p>(8c)</p>	532
<p>3-Hydroxymethylene-4-oxo-1,2,3,4-tetrahydrophenanthrene</p> <p>NaOCH_3</p>	 <p>(8c)</p>	<p>3,4-Di-(2-methoxyphenyl)-2-cyclohexen-1-one (52-53)</p>	533
<p>$(\text{CH}_3)_3\text{N} \cdot \text{CH}_3\text{I}$</p>	<p>2,2'-Dimethoxydeoxybenzoin</p> <p>NaOC_2H_5</p>	 <p>(9a)</p>	705
<p>$(\text{C}_2\text{H}_5)_3\text{N} \cdot \text{CH}_3\text{I}$</p>	<p>1-Hydroxymethylene-3-methyl-anilinoethylene-trans-2-decalone</p> <p>NaOCH_3</p>		691

Note: References 491-1045 are on pp. 545-555.
 || This is the structure assumed by the authors.

TABLE VIII—Continued

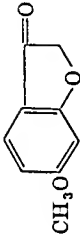
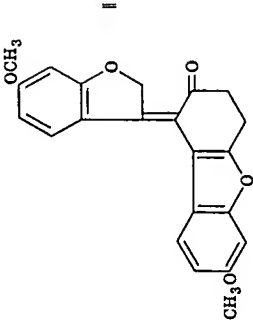

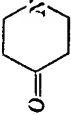
ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES	Substituent R in $\text{CH}_3\text{COCH}_2\text{CH}_2\text{R}$	Addend	Catalyst	Product (Yield, %) $A = \text{CH}_3\text{COCH}_2\text{CH}_2-$	References
	$(\text{C}_2\text{H}_5)_2\text{N} \cdot \text{CH}_3\text{I}$ (<i>Cont.</i>)	2-Methylcyclopentane-1,3-dione	NaOCH_3	 (37)	528, 706
		Cyclohexane-1,3-dione	Piperidine		532
		2-Methylcyclohexane-1,3-dione	None		663
			NaOCH_3 ; NaNH_2 ; $(\text{C}_2\text{H}_5)_2\text{NH}$; pyridine; NaOC_2H_5		663, 706, 707

$(C_3H_5)_3N$	$NaOC_2H_5$		528
$(C_3H_5)_3N$	None		538
$(C_3H_5)_3N \cdot CH_3I$	2-Methylcyclohexane-1,3-dione		708, 709
$(C_3H_5)_3N$	5,5-Dimethylcyclohexane-1,3-dione		538
$(CH_3)_4N$ $(C_4H_9)_4N$	Nitromethane 2-Nitropropane		710 691

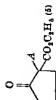
Note: References 191-1045 are on pp. 545-555.

† This compound is formed by ring fission of the primary product.

TABLE VIII—Continued
ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES

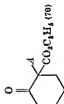
Substituent R in $\text{CH}_3\text{COCH}_2\text{CH}_2\text{R}$	Addend	Catalyst	Product (Yield, %) $A = \text{CH}_3\text{COCH}_2\text{CH}_2-$	References
$(\text{C}_2\text{H}_5)_2\text{N} \cdot \text{CH}_3\text{I}$		NaNH_2		711
	Methyl fluorene-9-carboxylate	KOH	Methyl 9-(β -acetylethyl)fluorene-9-carboxylate (45)	544
	Reactants $\text{NCH}_3\text{CH}_3\text{I}$ and	Catalyst	Product (Yield, %) $A = (\text{CH}_3)_2\text{NCH}_2\text{CH}_2\text{COCH}_2\text{CH}_2-$	References
Diethyl malonate	KOC_2H_5		$\text{ACH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (25)	681
Ethyl acetacetate	KOC_2H_5		$\text{CH}_3\text{COCH}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$	681

681

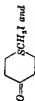
 KOC_2H_5

2-Carbethoxycyclopentanone

681

 KOC_2H_5

2-Carbethoxycyclohexanone

 $A = \text{CH}_3\text{SCH}_2\text{CH}_2\text{COCH}_2\text{CH}_2-$

Diethyl malonate

Dimethyl β keto- α -methyladipate $\Delta\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (42) $\text{CH}_3\text{O}_2\text{C}(\text{CH}_2)_4\text{COC}(A)(\text{CH}_2)_2\text{CO}_2\text{CH}_3$ (70)

712

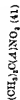
712

2-Carbethoxycyclopentanone

 KOC_2H_5 

712

2-Nitropropane

 KOC_2H_5 

712

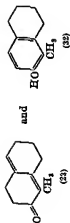
Note: References 491-1045 are on pp. 545-555.

|| This is the structure assumed by the authors.

TABLE VIII—Continued
ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES

Reactants	Catalyst	Product (Yield, %)	References
$CH_3CH_2COCH_2CH_2N(C_2H_5)_3 \cdot CH_3I$ and 2-Carbethoxycyclohexanone**	$NaOC_2H_5$	 Methyl 1-oxo-2-(β -propionylethyl)-1,2,3,4-tetra- hydronaphthalene-2-carboxylate (96)	231
Methyl 1-oxo-1,2,3,4-tetrahydronaphthalene-2- carboxylate	$NaOCH_3$	Methyl 4-oxo-3-(β -propionylethyl)-1,2,3,4-tetra- hydronaphthalene-3-carboxylate (87)	532
Methyl 4-oxo-1,2,3,4-tetrahydronaphthalene-3- carboxylate	$NaOCH_3$		533
Cyclohexane-1,3-dione	$(C_2H_5)_3N$	 (Enol)	115, 532
2-Hydroxycyclohexanone	None	 (Quant.)	713
2-Methylcyclohexanone	$NaNH_2$	 (28-38) and (Low)	714

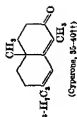
2-Acetoxybicyclohexanone

NaOCH₃

713

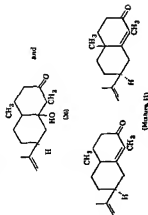
Carvenone

—



715

{+}-Dihydrocarvone

NaNH₂

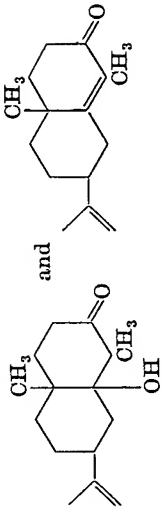
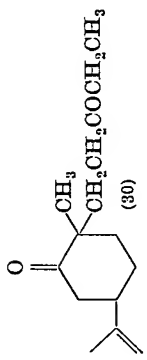
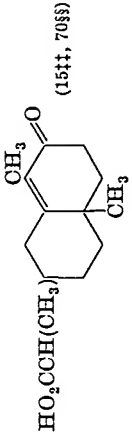
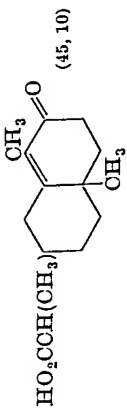
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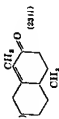
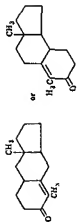

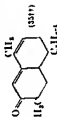
Note. References 491-1015* are on pp. 545-555.

** In this instance, the tertiary base was used instead of the quaternary methiodide.

†† This compound resulted from the treatment of the crude primary product with boiling potassium hydroxide solution.

TABLE VIII—Continued

ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES		References
Reactants	Catalyst	
$C_6H_5CH_2COCH_2CH_2N(C_2H_5)_2 \cdot CH_3I$ (Cont.) and (-)-Dihydrocarvone	$NaNH_2$	714
	Product (Yield, %)	
		
	$NaNH_2$	717
		
5-(α -Carbomethoxyethyl)-2-methylcyclohexanone	$NaOCH_3$	664, 718
		
	$NaNH_2$	188, 718
		

9 Methylhydrotan-8-one	$(C_8H_9)_2CN_2$		187
$CH_3(CH_2CH_2CH_2)_3CH_2I$ and ethyl isobutyrylacetate	$NaNH_2$		230
ethyl isobutyrylacetate	—		684
ethyl isobutyrylacetate	$NaOC_2H_5$	3,4,5-Trimethyl-2-cyclohexen-1-one (65)	100
Hydroxymethylacetophenone	$NaOH, H_2$		720

Note: References 101, 1015 are on pp. 615, 555.

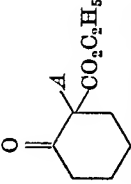
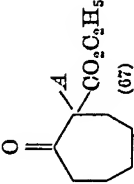
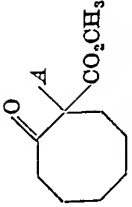
∴ This compound resulted from the treatment of the crude primary product with boiling potassium hydroxide solution.

∴ About two thirds of the keto ester failed to enter into the reaction.

(1) One quarter of the keto ester could be recovered unchanged.

The ester obtained in the reaction was hydrolyzed.

TABLE VIII—Continued
ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES

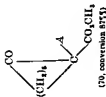
Reactants	Catalyst	Product (Yield, %)	References
$CH_3COCH[CH_2N(CH_3)_2 \cdot C_2H_5I]_2$ and 2-Carbethoxycyclohexanone	$NaOCH_3$	$A = CH_3COCHCH_2-\overset{CH_3}{\parallel}$  (74, conversion 65%)	689
2-Carbethoxycycloheptanone	$NaOCH_3$	 (67)	689
2-Carbomethoxycycloöctanone	$NaOCH_3$	 (66, conversion 89%)	689

2-Carbomethoxycyclohexanone

NaOCH₃

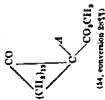
689

2-Carbomethoxycyclohexanone

NaOCH₃

689

2-Carbomethoxycyclohexanone

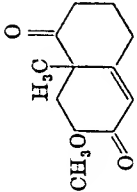
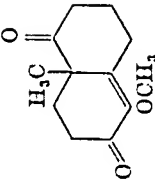
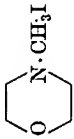


NaOCH₃

688

Note: References 491-1015 are on pp. 545-555.

99 (Only the indicated amount of the keto ester entered into the reaction; the balance could be recovered unchanged.)

TABLE VIII—Continued
ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES

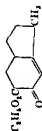
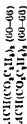
Reactants	Catalyst	Product (Yield, %)	References
$CH_3OCH_2COCH_2CH_2N(C_2H_5)_2$ and $CH_3COCH(OCH_3)CH_2N(C_2H_5)_2$ (mixture) and			
2-Methylcyclohexane-1,3-dione	Pyridine	 and 	721
Substituent R in $(CH_3)_2CHCOCH_2CH_2R$	Addend	Product (Yield, %)	References
$(CH_3)_2N$	Ethyl acetoacetate	3-Isopropyl-2-cyclohexen-1-one	722
	Ethyl methylacetoacetate	Carvenone (43)	100
Reactants	Catalyst	Product (Yield, %)	References
$(CH_3)_2CHCH_2COCH_2CH_2N$  $O \cdot CH_3I$ and			
Ethyl acetoacetate	$NaOC_2H_5$	3-Isobutyl-2-cyclohexen-1-one (45)	100
$(CH_3)_3CCOCH_2CH_2N$  $O \cdot CH_3I$ and			
Ethyl acetoacetate	$NaOC_2H_5$	3-4-Butyl-2-cyclohexen-1-one (45)	100

2-Diethylaminomethyl 3-methylcyclopentanone methiodide and

ethyl acetosuccinate



229

Diethyl malonate
Diethyl malonate114, 723
114, 723

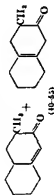
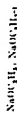
Ethyl acetosuccinate



724

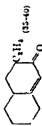
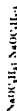


Ethyl methylacetosuccinate



725

Ethyl ethylacetosuccinate

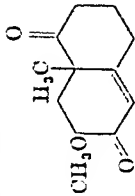
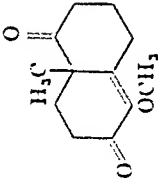
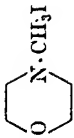

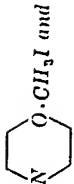




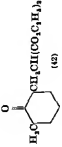
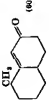
725

Note. References for 1015 are on pp. 545-555.

TABLE VIII—Continued

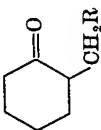
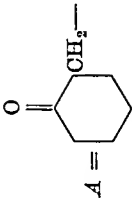
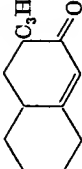
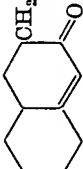
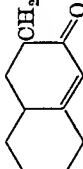
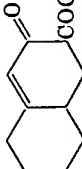
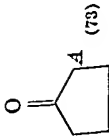
ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES

Reactants	Catalyst	Product (Yield, %)	References
$CH_3OCH_2COCH_2CH_2N(C_2H_5)_2$ and $CH_3COCH(OCH_3)CH_2N(C_2H_5)_2$ (mixture) and			
2-Methylcyclohexane-1,3-dione	Pyridine	 and 	721
Substituent R in $(CH_3)_2CHCOCH_2CH_2R$	Addend	Product (Yield, %)	References
$(CH_3)_2N$	Ethyl acetate	—	722
	Ethyl methylacetate	Carvenone (43)	100
Reactants	Catalyst	Product (Yield, %)	References
$(CH_3)_2CHCH_2COCH_2CH_2N$  $O \cdot CH_3I$ and			
Ethyl acetate	$NaOC_2H_5$	3-Isobutyl-2-cyclohexen-1-one (45)	100
$(CH_3)_2CCOCH_2CH_2N$  $O \cdot CH_3I$ and			
Ethyl acetate	$NaOC_2H_5$	3- <i>t</i> -Butyl-2-cyclohexen-1-one (45)	100

Hexane-2,5-dione	None		691
Cyclohexanone	None		691
Nitromethane	NaOC_2H_5	$\Delta\text{CH}_3\text{NO}_2$	710
Nitroethane	NaOC_2H_5	$\Delta\text{CH}(\text{CH}_3)\text{NO}_2$	726
1-Nitropropane	NaOH	$\Delta\text{CH}(\text{C}_2\text{H}_5)\text{NO}_2$ (78)	691
2-Nitropropane	NaOH	$(\text{CH}_3)_2\text{CH}\Delta\text{NO}_2$ (81)	691
Reactants	Catalyst	Product (Yield, %)	References
<i>2-Diethylaminomethyl-6-methylcyclohexanone Methiodide and</i>			
Diethyl malonate	NaOC_2H_5		114
Ethyl acetoacetate	NaOC_2H_5		229

Note: References 491-1015 are on pp. 545-555.

TABLE VIII—Continued
ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES

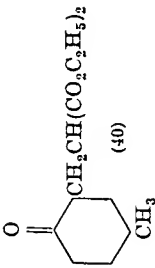
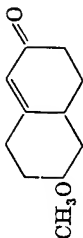
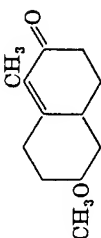

Substituent R in	Addend	Catalyst	Product (Yield, %)	References
			 A =	
$(\text{CH}_3)_3\text{N} \cdot \text{CH}_3\text{I}$ (Cont.)	Ethyl n-propylacetoacetate	NaOC_2H_5	 $\text{C}_3\text{H}_7\text{-}n$ (30-35)	725
	Ethyl allylacetoacetate	NaOC_2H_5	 $\text{CH}_2\text{CH}=\text{CH}_2$ (20)	726
	Ethyl phenylacetoacetate	NaOC_2H_5	$\text{CH}_3\text{COC}(A)(\text{C}_6\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5$	725
	Ethyl benzylacetoacetate	NaOC_2H_5	 $\text{CH}_2\text{C}_6\text{H}_5$ (35-40)	725
	Acetylacetone	None	 COCH_3 (60)	691
$(\text{CH}_3)_2\text{N}$	Cyclopentanone	None	 A (73)	691







				727, 728
Ethyl acetoacetate	NaOC_2H_5		(69)	
6-Dimethylaminomethyl 3-methyl 2-cyclohexen-1-one Methiodide and				
Ethyl acetoacetate	—			682
Ethyl propionylacetate	—			682
Ethyl 7-piperidino-5-oxoheptanoate and				
2-Methylcyclohexane-1,3 dione	Pyridine		(30-55)	708
			(Low)	

Note: References 491-1045 are on pp 545-555

*** This compound is formed by ring fission of the primary product and recyclization. When the methiodide of ethyl 7-piperidino-5-oxoheptanoate was employed in conjunction with sodium methoxide, the dibasic acid was the main product of the reaction

TABLE VIII—Continued
ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES

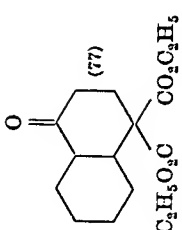
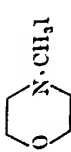
Reactants	Catalyst	Product (Yield, %)	References
2-Diethylaminomethyl-4-methylcyclohexanone Methiodide and			
Diethyl malonate	NaOC_2H_5	 <p>(40)</p>	114
2-Diethylaminomethyl-4-methoxycyclohexanone Methiodide and			
Ethyl acetate	NaOC_2H_5		697
Ethyl β -oxovalerate	NaOC_2H_5		697
 Diethyl malonate	NaOC_2H_5	Diethyl 2-(2'-oxocycloheptyl)ethane-1,1-dicarboxylate	727








$(\text{CH}_3)_2\text{N}$	Cyclopentanone	None		691
	Cyclopentanone	None		691
$(\text{CH}_3)_4\text{N}$	Acetylacetone	None	6-Acetyl-3-phenyl-2-cyclohexen-1-one (50)	691
	Cyclohexanone	$\text{NaOH}, \text{C}_2\text{H}_5\text{OH}$		731
		None		691
	Cyclohexanone	None		691

Note: References 491-1045 are on pp. 545-555.

TABLE VIII—Continued

ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES

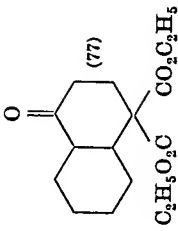
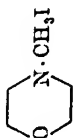
Reactants	Catalyst	Product (Yield, %)	References	
<i>β-Dimethylaminoethyl Cyclohexyl Ketone Hydrochloride and</i>				
Methyl acetate	$\text{KOC}_4\text{H}_9\text{-}t$	3-Cyclohexyl-2-cyclohexen-1-one (30)	729	
<i>1-(β-Dimethylaminopropionyl)-1-cyclohexene Hydrochloride and</i>				
Methyl acetate	$\text{KOC}_4\text{H}_9\text{-}t$	4-Acetyl-4-carbomethoxy-1-decalone (47)	729	
<i>1-(β-Morpholinopropionyl)-1-cyclohexene Methylide and</i>				
Diethyl malonate	NaOC_2H_5	 (77)	100	
Substituent R in $\text{RCH}_2\text{CH}_2\text{COC}_6\text{H}_5$	Addend	Catalyst	Product (Yield, %)	References
$(\text{CH}_3)_2\text{N} \cdot \text{HCl}$	Methyl acetate	$\text{KOC}_4\text{H}_9\text{-}t$	$\text{A} = -\text{CH}_2\text{CH}_2\text{COC}_6\text{H}_5$	
	Ethyl acetate	$\text{KOC}_4\text{H}_9\text{-}t$	3-Phenyl-2-cyclohexen-1-one (60)	729
$(\text{CH}_3)_2\text{N}$	Ethyl acetate	NaOC_2H_5	3-Phenyl-2-cyclohexen-1-one (60)	730
			6-Carbethoxy-3-phenyl-2-cyclohexen-1-one	574
	Ethyl acetate	NaOC_2H_5	3-Phenyl-2-cyclohexen-1-one (60)	100

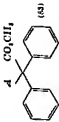
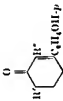
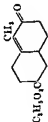
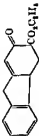
$(\text{CH}_3)_3\text{N}$	Cyclopentanone	None	 (95)	691
	Cyclopentanone	None	 (83)	691
$(\text{CH}_3)_3\text{N}$	Acetylacetone	None	6-Acetyl-3-phenyl-2-cyclohexen-1-one (50)	691
	Cyclohexanone	$\text{NaOH}, \text{C}_2\text{H}_5\text{OH}$	 (50)	731
		None	 (95)	691
	Cyclohexanone	None	 (73)	691

Note: References 491-1045 are on pp. 545-555.

TABLE VIII—Continued


ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES

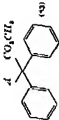


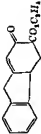
Reactants	Catalyst	Product (Yield, %)	References
<i>β-Dimethylaminooethyl Cyclohexyl Ketone Hydrochloride and Methyl acetoneacetate</i>	$\text{KOC}_4\text{H}_9\text{-}t$	3-Cyclohexyl-2-cyclohexen-1-one (30)	729
<i>1-(β-Dimethylaminopropionyl)-1-cyclohexene Hydrochloride and Methyl acetoneacetate</i>	$\text{KOC}_4\text{H}_9\text{-}t$	4-Acetyl-4-carbomethoxy-1-decalone (47)	729
<i>1-(β-Morpholinopropionyl)-1-cyclohexene Methiodide and Diethyl malonate</i>	NaOC_2H_5	 (77)	100
Substituent R in $\text{RCH}_2\text{CH}_2\text{COC}_6\text{H}_5$	Addend	Product (Yield, %)	References
$(\text{CH}_3)_2\text{N} \cdot \text{HCl}$	Methyl acetoneacetate	$A = -\text{CH}_2\text{CH}_2\text{COC}_6\text{H}_5$	
	Ethyl acetoneacetate	3-Phenyl-2-cyclohexen-1-one (60)	729
$(\text{CH}_3)_2\text{N}$	Ethyl acetoneacetate	3-Phenyl-2-cyclohexen-1-one (60)	730
	Ethyl acetoneacetate	6-Carboethoxy-3-phenyl-2-cyclohexen-1-one	574
		3-Phenyl-2-cyclohexen-1-one (60)	100

Reactants	Catalyst	Product (Yield, %)	References
$(C_2H_5)_4N \cdot (CH_3)_2SO_4$ Methyl fluorene-9-carboxylate KOH			514
β -Dimethylamino-p-hydroxypropylphenone Hydrochloride and			
Ethyl acetoacetate	KOC ₂ H ₅ -4		729
Ethyl ethylacetoacetate	KOC ₂ H ₅ -4	R' = R'' = H (30)	729
Ethyl isopropylacetoacetate	KOC ₂ H ₅ -4	R' = C ₃ H ₇ , R'' = H (71)	729
Ethyl α -propionylpropionate	KOC ₂ H ₅ -4	R' = (CH ₃) ₂ CH and CO ₂ C ₂ H ₅ , R'' = H (30)	729
Ethyl α , γ -diphenylacetoacetate	KOC ₂ H ₅ -4	R' = R'' = CH ₃ (50)	729
Acetylacetone	KOC ₂ H ₅ -4	R' = R'' = C ₆ H ₅ (15)	729
	KOC ₂ H ₅ -4	R' = CH ₃ CO, R'' = H (12)	729
4-Carbethoxy-2-dichloraminomethylcyclohexanone Methiodide and			
Ethyl β -oxovalerate	NaOC ₂ H ₅		697
2-Morpholinomethyl-1-hydrindone Methiodide and*			
Ethyl acetoacetate	NaOC ₂ H ₅		732

Note: References 491-1045 are on pp. 545-555.

TABLE VIII—Continued
ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES

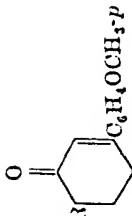
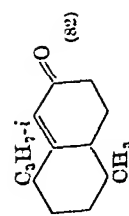
Substituent R in $RCH_2CH_2COC_6H_5$	Addend	Catalyst	Product (Yield, %)	References
$(CH_3)_2N$			$A = -CH_2CH_2COC_6H_5$	
	Hexane-2,5-dione	None	6-Acetyl-1-3-phenyl-2-cyclohexen-1-one (22)	691
	Acetophenone	None	$A_2CH_2COC_6H_5$ (40)	691
	Deoxybenzoin	None	$C_6H_5CH(A)COC_6H_5$ (9)	691
	Nitromethane	$NaOC_2H_5$	$A_2CH_2NO_2$, $(A)_2CHNO_2$, $(A)_3CNO_2$	710
		$NaOH$	$A_2CH_2NO_2$ (13)	691
		None	$A_2CH_2NO_2$ (15)	691
	Nitroethane	$NaOH$	$A_2CH(CH_3)NO_2$ (7) and $A_2C(CH_3)NO_2$ (50)	691
$(C_2H_5)_2N$				
	Nitroethane	$NaOH$	$A_2C(CH_3)NO_2$ (30)	691
$(CH_3)_2N$				
	1-Nitropropane	$NaOC_2H_5$	$A_2CH(CH_3)NO_2$ (48) and $A_2C(CH_3)NO_2$ (30)	691
	1-Nitropropane	$NaOH$	$A_2CH(C_2H_5)NO_2$ (80)	691
	2-Nitropropane	$NaOC_2H_5$	$A_2CH(C_2H_5)NO_2$ (60)	691
		$NaOH$	$(CH_3)_2C(A)NO_2$ (12)	691
				
	2-Nitropropane	$NaOH$	$(CH_3)_2C(A)NO_2$ (84)	691
$(CH_3)_2N$				
	1-Nitro-2-phenylethane	$NaOH$	$C_6H_5CH_2CH(A)NO_2$ (68) and $C_6H_5CH_2C(A)_2NO_2$ (7)	691

$(C_6H_5)_3N \cdot (CH_3)_3SO$, Methyl fluorane- β -carboxylate KOH			511
Reactants	Catalyst	Product (Yield, %)	Reference
β -Dimethylamino- p -hydroxypropophenone Hydrochloride and			
Ethyl acetoacetate	KOC ₂ H ₅ , t	R' = R'' = H (30)	729
Ethyl ethylacetoacetate	KOC ₂ H ₅ , t	R' = C ₂ H ₅ , R'' = H (71)	729
Ethyl isopropylacetoacetate	KOC ₂ H ₅ , t	R' = (CH ₃) ₂ CH and CO ₂ C ₂ H ₅ , R'' = H (30)	729
Ethyl α -propionylpropionate	KOC ₂ H ₅ , t	R' = R'' = CH ₃ (50)	729
Ethyl α , γ -diphenylacetoacetate	KOC ₂ H ₅ , t	R' = R'' = C ₆ H ₅ (15)	729
Acetylacetone	KOC ₂ H ₅ , t	R' = CH ₃ CO, R'' = H (12)	729
4-Carboethoxy-2-dimethylaminomethylcyclohexanone Methiodide and			
Ethyl β -oxovalerate	NaOC ₂ H ₅		607
2-Morpholinomethyl-1-hydrindone Methiodide and			732
Ethyl acetoacetate	NaOC ₂ H ₅		

Note. References 491-1045 are on pp. 545-555.

TABLE VIII—Continued
ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES

ROBINSON'S MODIFICATION

Reactants	Catalyst	Product (Yield, %)	References
<i>β-Dinethylaminoethyl <i>p</i>-Methoxyphenyl Ketone Hydrochloride and</i>			
Ethyl acetoacetate	$\text{KOC}_4\text{H}_9\text{-}t$		729
Ethyl ethylacetoacetate	$\text{KOC}_4\text{H}_9\text{-}t$		729
Ethyl isopropylacetoacetate	$\text{KOC}_4\text{H}_9\text{-}t$		729
Acetylacetone	$\text{KOC}_4\text{H}_9\text{-}t$		729
Nitromethane†††	$\text{KOC}_4\text{H}_9\text{-}t$		710
<i>β-Dinethylaminoisopropyl Phenyl Ketone Hydrochloride and</i>			
Ethyl acetoacetate	$\text{KOC}_4\text{H}_9\text{-}t$	4-Methyl-3-phenyl-2-cyclohexen-1-one (40, 38)	729, 730
<i>β-Morpholino-α-phenylethyl Methyl Ketone and</i>			
2-Nitropropane	NaOH	2-Methyl-2-nitro-4-phenylhexan-5-one (89)	691
<i>6-Isopropyl-3-methyl-2-morpholinomethylcyclohexan-1-one Methylide and</i>			
Ethyl acetoacetate	NaOC_2H_5		733



2-Dimethylaminomethyl-1-tetralone and

Ethyl acetacetate	NaOC_2H_5	$\text{R} = \text{H}$	724
Ethyl methylacetacetate	NaOC_2H_5	$\text{R} = \text{CH}_3$	724

 β -Dimethylamino- α -(p-methoxyphenyl)ethyl Methyl Ketone Methiodide and

2-Hydroxymethylene-8-methoxy-1-tetralone	NaOCH_3	2-(p-Methoxyphenyl)-3-oxo-7-methoxy-1,2,3,9,10,10a-hexahydrophenanthrene (46)	734
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3,4-Dimethoxyphenyl β -Dimethylaminomethyl Ketone and Nitromethane

NaOC_2H_5	1-(3',4'-Dimethoxyphenyl)-4-nitrobutan-1-one	710
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 β -Dimethylamino- β -(p-methoxyphenyl)ethyl Methyl Ketone and Nitromethane

NaOC_2H_5	4-(p-Methoxyphenyl)-5-nitropentan-2-one	710
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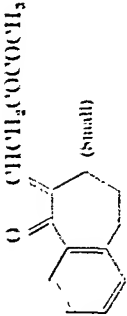
 β -Dimethylamino- β -(3,4-dimethoxyphenyl)ethyl Methyl Ketone and Nitromethane

NaOC_2H_5	4-(3',4'-Dimethoxyphenyl)-5-nitropentan-2-one	710
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Note: References 491-1045 are on pp. 545-555.

††† The free base was employed, instead of the hydrochloride.

TABLE VIII—Continued
ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES

Reactants	Catalyst	Product (Yield, %)	References
β -Dimethylamino- β -(3,4-methylenedioxyphenyl)ethyl Methyl Ketone and Nitromethane	NaOC_2H_5	4-(3',4'-Methylenedioxyphenyl)-5-nitropentan-2-one	710
2-Dimethylaminomethylbenzosuberone and			394
Diacetyl mono dimethyl ketal	Na enolate		
β -Dimethylaminoethyl 4-Methoxy-2-naphthyl Ketone Hydrochloride and Methyl acetate	$\text{KOH}, (\text{C}_2\text{H}_5)_2\text{CHOH}$	3-(6'-Methoxy-2'-naphthyl)cyclohexen-1-one (70)	735
β -Dimethylamino- β -phenylethyl 2-Nitro-4,5-dimethoxyphenyl Ketone and Nitromethane	NaOC_2H_5	4-Nitro-1-(2'-nitro-4',5'-dimethoxyphenyl)-3-phenylbutan-1-one	710

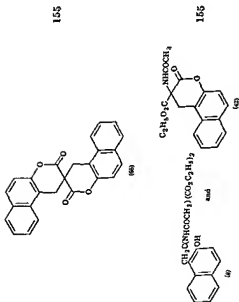


Addend

Catalyst

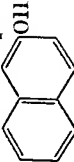
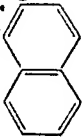

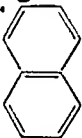
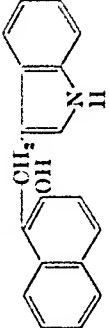
Product (Yield, %)




References



Note: References 491-1015 are on pp. 515-555.


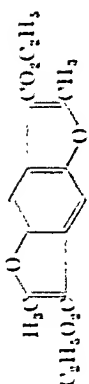
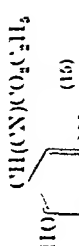
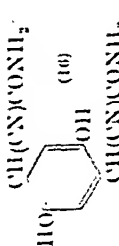
TABLE VIII—Continued
ROBINSON'S MODIFICATION OF THE MICHAEL CONDENSATION OF α,β -ETHYLENIC KETONES

Substituent R in	Addend	Catalyst	Product (Yield, %)	References
CH_2R 			$\text{CH}_2\text{CH}(\text{CO}_2\text{H})_2$  (53)	736, cf. 737, 738
	Dibenzoylmethane	$\text{HCl}, \text{C}_2\text{H}_5\text{OH}$		
$\text{C}_2\text{H}_5\text{S}$	2-Nitropropane	NaOH	$\text{CH}_2\text{C}(\text{NO}_2)(\text{CH}_3)_2$  (50)	155
	Indole	KOH	 (52)	155
Substituent R in $\text{RCH}_2\text{CH}(\text{NO}_2)\text{CH}_3$ $(i\text{-C}_3\text{H}_7)_2\text{N}$	Diethyl malonate	NaOC_2H_5 NaOC_2H_5 $[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	$A = \text{CH}_2\text{CH}(\text{NO}_2)\text{CH}_2---$ $\text{ACH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (37) $\text{ACH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (25) $\text{ACH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (47)	251 251 251

	Diethyl malonate	NaOC_2H_5	$\text{ACH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (13)	251
$(i\text{-C}_3\text{H}_7)_2\text{N}$	Ethyl acetoacetate	NaOC_2H_5 ; NaOC_4H_9	$\text{CH}_3\text{COCH}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (46)	251
	Ethyl acetoacetate	NaOC_2H_5	$\text{CH}_3\text{COCH}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (17)	251
$(i\text{-C}_3\text{H}_7)_2\text{N}$	Ethyl α -acetylsuccinate	NaOC_4H_9	$\text{C}_2\text{H}_5\text{O}_2\text{CC}(\text{A})\text{COCH}_3$ (72)	251
	Ethyl α -acetylsuccinate	NaOC_4H_9	$\text{C}_2\text{H}_5\text{O}_2\text{CC}(\text{A})\text{COCH}_3$ (8)	251
$(i\text{-C}_2\text{H}_5)_2\text{N}$	1-Nitropropane	$[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$ NaOH	$\text{CH}_3\text{CH}_2\text{CH}(\text{A})\text{NO}_2$ (33)	251
	2-Nitropropane	$[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$ NaOH	$\text{CH}_3\text{CH}_2\text{CH}(\text{A})\text{NO}_2$ (50) $(\text{CH}_3)_2\text{C}(\text{A})\text{NO}_2$ (52) $(\text{CH}_3)_2\text{C}(\text{A})\text{NO}_2$ (43)	251 251 251
Substituent R in $\text{RCH}_2\text{CH}(\text{NO}_2)\text{CH}_2\text{CH}_2$				
$(\text{CH}_3)_2\text{N}$	1-Nitropropane	NaOH	$\text{A} = \text{CH}_2\text{CH}_2\text{CH}(\text{NO}_2)\text{CH}_2$ — $\text{CH}_2\text{CH}_2\text{CH}(\text{A})\text{NO}_2$ (34)	251, 739
$(\text{C}_2\text{H}_5)_2\text{N}$	1-Nitropropane	NaOH	$\text{CH}_2\text{CH}_2\text{CH}(\text{A})\text{NO}_2$ (18)	251, 739
$(i\text{-C}_3\text{H}_7)_2\text{N}$	1-Nitropropane	$[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$ NaOH	$\text{CH}_2\text{CH}_2\text{CH}(\text{A})\text{NO}_2$ (15)	251
$(\text{CH}_3)_2\text{N}$	2-Nitropropane	NaOH	$\text{CH}_2\text{CH}_2\text{CH}(\text{A})\text{NO}_2$ (18)	251, 739
$(i\text{-C}_3\text{H}_7)_2\text{N}$	2-Nitropropane	$[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$ NaOH	$(\text{CH}_3)_2\text{C}(\text{A})\text{NO}_2$ (55) $(\text{CH}_3)_2\text{C}(\text{A})\text{NO}_2$ (50) $(\text{CH}_3)_2\text{C}(\text{A})\text{NO}_2$ (44)	251 251 251

Note: References 491-1015 are on pp. 545-555.

TABLE IX
MICHAEL CONDENSATIONS WITH QUINONES AND THEIR DERIVATIVES

Reactants	Catalyst	Product (Yield, %)	References
<i>p</i> -Benzophenone and Ethyl acetate	ZnCl ₂ (1)		256
CH ₃ C(=NH)CH(CH ₃)(CO ₂ C ₂ H ₅)	None		377
C ₂ H ₅ OC(=NH)CH ₂ (CO ₂ C ₂ H ₅)	None	Ethyl 2-ethoxy-5-hydroxyindole-3-carboxylate (38)	377
Ethyl cyanoacetate	NH ₃ , ethanol		252
Cyanoacetamide	NH ₃ , ethanol		252

Malononitrile

 NH_3 , ethanol

252

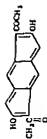
Acetylacetone

Pyridine



740

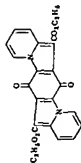
2,6-Dichlorobenzoquinone and



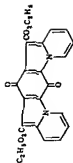
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Ethyl acetoacetate

Pyridine

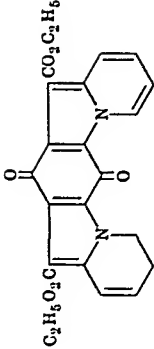
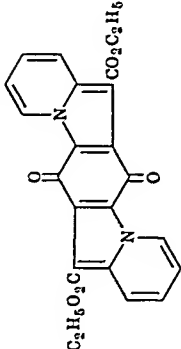
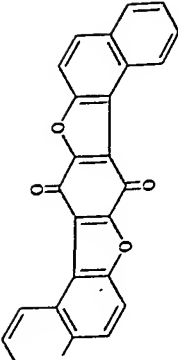


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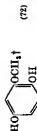
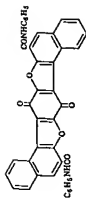


Note: References 491-1045 are on pp. 545-555.
 * This is the formula assumed by the author.

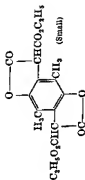
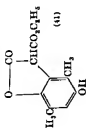
TABLE IX—Continued

MICHAEL CONDENSATIONS WITH QUINONES AND THEIR DERIVATIVES	Product (Yield, %)	References
Catalyst		
Reactants <i>Chloranil and</i>	 <chem>O=C1C(=C(C(=C1C(=O)C2=CC=CC=C2)C3=CC=CC=C3)C4=CC=CC=C4)C5=CC=CC=C5</chem>	272
Ethyl acetate	 <chem>O=C1C(=C(C(=C1C(=O)C2=CC=CC=C2)C3=CC=CC=C3)C4=CC=CC=C4)C5=CC=CC=C5</chem>	272
β -Naphthol	 <chem>O=C1C(=O)C2=CC=CC=C2OC3=CC=CC=C3C1=CC=C2</chem>	272
Pyridine		

2-Hydroxy-3-naphthanilide	Pyridine	272
<i>Methoxybenzoquinone and</i>		
$\text{CH}_3\text{C}(=\text{NH})\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$	None	377
$\text{C}_6\text{H}_4\text{OC}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	None	377
<i>p</i> -Xyloquinone and		
Diethyl malonate	NaOC_2H_5	742

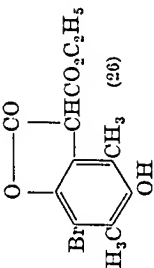
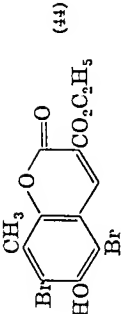
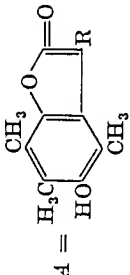
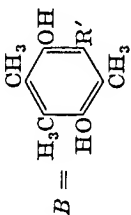
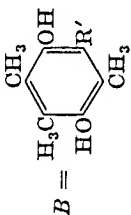
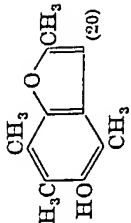


Elhyl 2 ethoxy-5-hydroxy-6-methoxyindole-3-carboxylate† (46)



Note. References 491-1045 are on pp. 515-555.

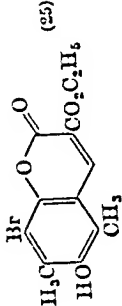
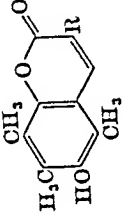
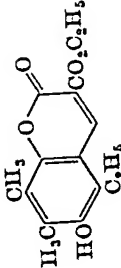
† The position of the methoxyl group has not been determined.

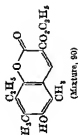
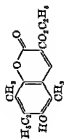
TABLE IX—Continued			
Reactants	Catalyst	Product (Yield, %)	References
<i>2-Bromo-3,5-dimethylbenzoquinone and</i>			
Diethyl malonate	NaOC_2H_5	 (26)	743
<i>3,5-Dibromo-2,6-dimethylbenzoquinone and</i>			
Diethyl malonate	Na	 (44)	744
<i>Trimethylbenzoquinone and</i>			
Diethyl malonate	NaOC_2H_5	 A =  B =  	253, 745
Ethyl acetoneacetate	NaOC_2H_5 ; Na	 (20)	745
Ethyl palmitoylacetate	NaOC_2H_5	A, R = COCH_3 (55)	745
Ethyl stearoylacetate	NaOC_2H_5	A, R = $\text{COC}_{13}\text{H}_{31-n}$	746
		A, R = $\text{COC}_{17}\text{H}_{35-n}$ (27)	746

Diethyl isobutyrylmalonate Ethyl cyanoacetate	NaOC_2H_5 ; Na	$\text{Mg}(\text{OC}_2\text{H}_5)_2$	$A, R = \text{CO}_2\text{C}_2\text{H}_5$ (50) Ethyl trimethylthioquinonecyanacetate (32)	253 388
Trimethylbenzoquinone and			$A = \begin{array}{c} \text{CH}_3 \\ \\ \text{H}_3\text{C} \text{---} \text{O} \text{---} \text{C} \text{---} \text{O} \text{---} \text{H} \\ \quad \quad \\ \text{HO} \quad \quad \text{CH}_3 \end{array}$ $B = \begin{array}{c} \text{CH}_3 \\ \\ \text{H}_3\text{C} \text{---} \text{O} \text{---} \text{C} \text{---} \text{O} \text{---} \text{H} \\ \quad \quad \\ \text{HO} \quad \quad \text{CH}_3 \end{array}$	
Cyanoacetamide	NaOCH_3		$A = \begin{array}{c} \text{CH}_3 \\ \\ \text{H}_3\text{C} \text{---} \text{O} \text{---} \text{C} \text{---} \text{O} \text{---} \text{H} \\ \quad \quad \\ \text{HO} \quad \quad \text{CH}_3 \end{array}$ $B = \begin{array}{c} \text{CH}_3 \\ \\ \text{H}_3\text{C} \text{---} \text{O} \text{---} \text{C} \text{---} \text{O} \text{---} \text{H} \\ \quad \quad \\ \text{HO} \quad \quad \text{CH}_3 \end{array}$	388
Benzyl cyanide	NaOCH_3		$A, R = \text{C}_6\text{H}_5$ (32)	
Acetylacetone	NaOC_2H_5		$B, R' = \text{CH}_3\text{COCH}_2\text{COCH}_3$ (72)	398
Isobutyrylacetone	NaOC_2H_5		$B, R' = \text{CH}_3\text{COCH}_2\text{COCH}_3$ (72)	259
2,6-Dimethylheptane-3,5-dione	NaOC_2H_5		$B, R' = \text{CH}_3\text{COCH}_2\text{COCH}_3$ (72)	259
Heptadecane-2,4 dione	NaOC_2H_5		$B, R' = \text{CH}_3\text{COCH}_2\text{COCH}_3$ (72)	260
5,9,13,17-Tetramethyloctadecane 2,4-dione	NaOC_2H_5		$B, R' = \text{CH}_3\text{COCH}_2\text{COCH}_3$ (72)	254
Acetomesitylene		Bromomagnesium enolate	$B, R' = \text{C}_6\text{H}_4(\text{CH}_3)_2$ (90)	253

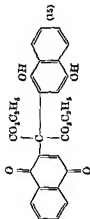
Note: References 491-1045 are on pp. 545-555.

TABLE IX—Continued
MICHAEL CONDENSATIONS WITH QUINONES AND THEIR DERIVATIVES

Reactants	Catalyst	Product (Yield, %)	References
<i>Bromotrimethylbenzoquinone and</i> <i>Diethyl malonate</i>	NaOC_2H_5		747
<i>Duroquinone and</i> <i>Diethyl malonate</i>	Na		201, cf. 747a, 747b
<i>Diethyl malonate</i>	Na	$\text{R} = \text{CO}_2\text{C}_2\text{H}_5$	203
<i>Ethyl acetoacetate</i>	Na	$\text{R} = \text{COCH}_3$ (25)	262
<i>Methyl cyanoacetate</i>	Na	$\text{R} = \text{CN}$ (26)	
<i>Trimethylglylbenzoquinone and</i> <i>Diethyl malonate</i>	Na		748

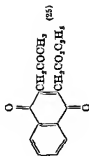


(Mixture, 90)



Pyridine

267



NaOH, ethanol

268

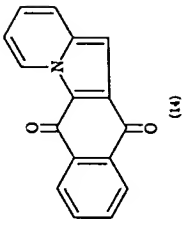
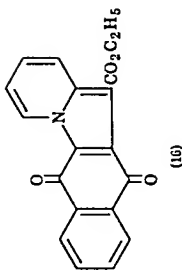
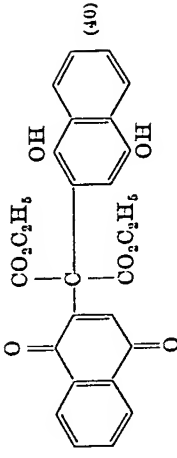
1,4-Naphthoquinone and

Diethyl malonate

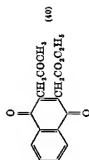
Ethyl acetoacetate

Note: References 491-1045 are on pp. 545-555.

TABLE IX—Continued
MICHAEL CONDENSATIONS WITH QUINONES AND THEIR DERIVATIVES

Reactants	Catalyst	Product (Yield, %)	References
1,4- <i>N</i> -aphthoquinone (Cont.) and			
Ethyl acetoneacetate (Cont.)	Pyridine, pyridine hydrochloride	 (14)	266
Ethyl benzoylacetate	Pyridine, pyridine hydrochloride	 (16)	269
Potassium 1,4-naphthoquinone-2-sulfonate and			
Diethyl malonate	Pyridine	 (40)	267

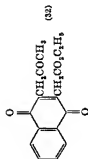
205

(CH₃)₄NOH

Ethyl acetate

2-Bromo-1,4-naphthoquinone and

206

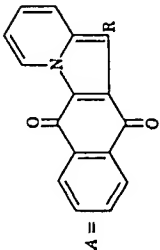
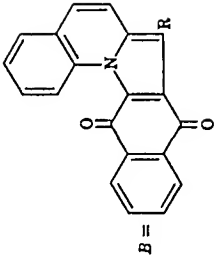
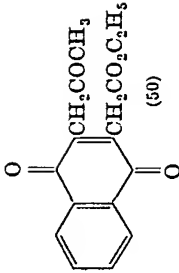


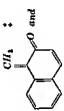

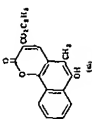
KOH, aq. ethanol

Ethyl acetate

TABLE IX—Continued

MICHAEL CONDENSATIONS WITH QUINONES AND THEIR DERIVATIVES

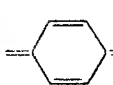
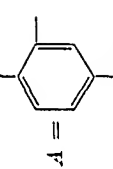
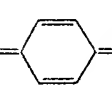
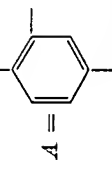
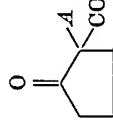
Reactants	Catalyst	Product (Yield, %)	References
2,3-Dichloro-1,4-naphthoquinone and		 A =  B =	
Dimethyl malonate	Quinoline, quinoline hydrochloride	B, R = CO ₂ CH ₃ (20)	266
Diethyl malonate	Pyridine	A, R = CO ₂ C ₂ H ₅ (6)	269
	Quinoline, quinoline hydrochloride	B, R = CO ₂ C ₂ H ₅ (11)	266
Methyl acetacetate	Pyridine, pyridine hydrochloride	A, R = CO ₂ CH ₃ (51)	266
	Quinoline, quinoline hydrochloride	B, R = CO ₂ CH ₃ (39)	266
Ethyl acetacetate	Pyridine, pyridine hydrochloride	A, R = CO ₂ C ₂ H ₅ (49, 62) or  (50)	266, 269
			266






Acetoacetanilide	Quinoline, quinoline hydrochloride	$R, R = CO_2C_2H_5$ (45)	260
Acetoacet- <i>o</i> -chloranilide	Pyridine	$A, R = COC_2H_5$ (31) and $A, R = CONHC_2H_5$ (8)	271, 272
Acetoacet- <i>o</i> -toluide	Pyridine	$A, R = COC_2H_5$	271, 272
2-(Acetoacetanido)-6-ethoxybenzothiazole	Pyridine	$A, R = COC_2H_5$	271, 272
Acetylacetone	Pyridine	$A, R = COC_2H_5$ (30)	269
Acetophenone	Pyridine	$A, R = COC_2H_5$ (13)	273
Dibenzoylmethane	Pyridine	$A, R = COC_2H_5$ (3)	273
 CH_3 ‡			
Diethyl malonate	Na		265
2,3-Dimethyl-1,4-naphthoquinone and			
Diethyl malonate	Na		749

Note: References 491-1015 are on pp. 545-555.

‡ This quinone was introduced as its diacet.

TABLE IX—Continued
MICHAEL CONDENSATIONS WITH QUINONES AND THEIR DERIVATIVES

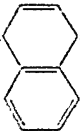
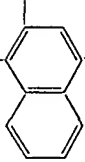






Reactants	Catalyst	Product (Yield, %)	References
NCOC_6H_5  <i>and</i> NCOC_6H_5 Diethyl malonate Acetylacetone	NaOCH_3 NaOCH_3	NHCOC_6H_5  $A =$ $\text{ACH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (76) $\text{CH}_3\text{COCH}(A)\text{COCH}_3$ (75)	749a 749a
$\text{NSO}_2\text{C}_6\text{H}_5$  <i>and</i> $\text{NSO}_2\text{C}_6\text{H}_5$ Diethyl malonate Ethyl acetoacetate	NaOCH_3 NaOCH_3	$\text{NHSO}_2\text{C}_6\text{H}_5$  $A =$ $\text{ACH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (57) $\text{CH}_3\text{COCH}(A)\text{CO}_2\text{C}_2\text{H}_5$ (90 crude)	750 750
2-Carboethoxycyclopentanone	NaOCH_3	 (97 crude)	750
Ethyl benzoylacetate	NaOCH_3	$\text{C}_6\text{H}_5\text{COCH}(A)\text{CO}_2\text{C}_2\text{H}_5$ (94 crude)	750
Acetylacetone	NaOCH_3	$\text{CH}_3\text{COCH}(A)\text{COCH}_3$ (25 crude)	750

Cyclohexane-1,3-dione	NaOCH_3		750
$\text{NSO}_2\text{C}_6\text{H}_5$ and 	Diethyl malonate Ethyl acetoacetate Acetylacetone		750 750 750
$\text{NSO}_2\text{C}_6\text{H}_5$ and 	NaOCH_3 NaOCH_3 NaOCH_3		750 750 750

Note: References 491-1015 are on pp. 545-555.

5 With this compound, ethyl cyanoacetate, malononitrile, nitromethane, nitroethane and 2-nitropropane gave only tarry products.

TABLE IX—Continued
MICHAEL CONDENSATIONS WITH QUINONES AND THEIR DERIVATIVES



Reactants	Catalyst	Product (Yield, %)	References
$\text{NSO}_2\text{C}_6\text{H}_5$  and $\text{NSO}_2\text{C}_6\text{H}_5$	Diethyl malonate Ethyl benzoylacrylate Acetylacetone Nitromethane Nitroethane	 $A =$	751 751 751 751 751
NCOC_6H_5  and NCOC_6H_5 Diethyl malonate Acetylacetone	$(\text{C}_2\text{H}_5)_3\text{N}$ $(\text{C}_2\text{H}_5)_3\text{N}$ $(\text{C}_2\text{H}_5)_3\text{N}$ $(\text{C}_2\text{H}_5)_3\text{N}$ $(\text{C}_2\text{H}_5)_3\text{N}$	$A =$  $A =$  $A =$ 	752 752
Cl  and NCOC_6H_5 Acetylacetone	NaOCH_3 NaOCH_3	 $\text{CH}(\text{COCH}_3)_2$	752

Note: References 491–1045 are on pp. 545–555.

‡ The position in which the substitution has taken place has not been determined.

¶ With diethyl malonate, this compound gave only an oily product.

TABLE X
MICHAEL CONDENSATIONS WITH ACRYLONITRILE*

Reactants	Catalyst	Product (Yield, %)	References
<i>A. Hydrocarbons</i>		$A = -CH_2CH_2CN$	
Cyclopentadiene	$[C_6H_5CH_2N(CH_3)_3]OH$	Hexa-(β -cyanoethyl)cyclopentadiene (9)	288
Indene	$[C_6H_5CH_2N(CH_3)_3]OH$	α,α -Bis-(β -cyanoethyl)indene (14)	288
		1,1,3-Tris-(β -cyanoethyl)indene 35)	
1-Isopropylideneindene	$[C_6H_5CH_2N(CH_3)_3]OH$	<div style="display: flex; align-items: center; justify-content: center;">  <div style="margin: 0 10px;">or</div>  <div style="margin-left: 10px;">(22)</div> </div>	288
Fluorene			
1-Methylfluorene	$[C_6H_5CH_2N(CH_3)_3]OH$	9,9-Di-(β -cyanoethyl)fluorene (74)	288, 753
2-Nitrofluorene	$[C_6H_5CH_2N(CH_3)_3]OH$	9,9-Di-(β -cyanoethyl)-1-methylfluorene (70)	482
2,7-Dibromofluorene	$[C_6H_5CH_2N(CH_3)_3]OH$	9,9-Di-(β -cyanoethyl)-2-nitrofluorene (70)	288
4,5-Methylenepheneanthrene	Not indicated	2,7-Dibromo-9,9 di-(β -cyanoethyl)fluorene	754
9-Phenylfluorene	$[C_6H_5CH_2N(CH_3)_3]OH$	4,5-(Di-(β -cyanoethyl)methylenepheneanthrene	754, 755
9-Fluoreneol	$[C_6H_5CH_2N(CH_3)_3]OH$	9-(β -Cyanoethyl)-9-phenylfluorene (73)	289
1,2,3,4-Tetrahydrofluoranthene	$[C_6H_5CH_2N(CH_3)_3]OH$	9-(β -Cyanoethyl)-9-fluoreneol	289
2,2,4-Trimethyl-1,2-dihydrofluoranthene	$[C_6H_5CH_2N(CH_3)_3]OH$	1-(β -Cyanoethyl)-1,2,3,4-tetrahydrofluoranthene	754, 755
		1-(β -Cyanoethyl)-2,2,4-trimethyl-1,2-dihydrofluoranthene	754, 755
<i>B. Aldehydes</i>		$A = -CH_2CH_2CN$	
Acetaldehyde	—	$(A)_3CHCHO, (A)_3CCHO$	756
Propionaldehyde	—	$CH_3CH(A)CHO, CH_3C(A)_2CHO$	756

Note: References 491-1045 are on pp. 545-555.

* Compare the review by Bruson.²¹

TABLE X—Continued
MICHAEL CONDENSATIONS WITH ACRYLONITRILE*

Reactants	Catalyst	Product (Yield, %)	References
<i>B. Aldehydes (Cont.)</i>			
Isobutyraldehyde	Quaternized polyvinyl- pyridine resin; aq. KCN	(CH ₃) ₂ C(A)CHO (40, 79) <i>A</i> = —CH ₂ CH ₂ CN	478, 759, 757
Diethylacetaldehyde	KOH, CH ₃ OH	(C ₂ H ₅) ₂ C(A)CHO (75-80)	278, 284
2-Ethyl-2-hexenal	KOH	CH ₃ CH ₂ CH=CHC(A)(C ₂ H ₅)CHO (50)	284
2-Ethylhexenal	KOH, CH ₃ OH	C ₄ H ₉ C(A)(C ₂ H ₅)CHO (75, 80)	278, 284
α -Phenylpropionaldehyde	KOH	(C ₆ H ₅)(CH ₃)C(A)CHO (74)	758
<i>C. Ketones</i>			
Acetone	Quaternized polyvinyl- pyridine resin NaOH	<i>A</i> = —CH ₂ CH ₂ CN CH ₃ COCH ₂ <i>A</i> (19) and CH ₃ COC(A) ₂ (32)	478
		CH ₃ COCH ₂ <i>A</i> (8), CH ₃ COCH(A) ₂ (14), CH ₃ COC(A) ₂ (24)	750
	[C ₂ H ₅ CH ₂ N(CH ₃) ₃]OH	CH ₃ COC(A) ₂ (75-80) and (A) ₂ CHCOC(A) ₂	700, 701
	[C ₂ H ₅ CH ₂ N(CH ₃) ₃]OH Na;	CH ₃ COCH ₂ <i>A</i> (18) [†]	702
	[C ₂ H ₅ CH ₂ N(CH ₃) ₃]OH KOH, C ₂ H ₅ OH;	CH ₃ COC(A) ₂ CH ₃ (51, 90) and (A) ₂ CHCOC(A) ₂ CH ₃	703, 701
Methyl ethyl ketone		CH ₃ COCH(A)CH ₃ (0, 20) and CH ₃ COC(A) ₂ CH ₃ (47) [‡]	275, 278
	[C ₂ H ₅ CH ₂ N(CH ₃) ₃]OH	CH ₃ COCH(A)CH ₃ and CH ₃ COC(A) ₂ CH ₃ (24-30) [†]	702
	[C ₂ H ₅ CH ₂ N(CH ₃) ₃]OH	CH ₃ COCH(A)CH ₃ and CH ₃ COC(A) ₂ CH ₃ (total, 47)	478
	Polyvinylpyridine resin Aq. KCN	CH ₃ COCH(A) ₂ CH ₂ CN (82)	123
Methyl β -cyanoethyl ketone	KOH, C ₂ H ₅ OH;	CH ₃ COCH(A)C ₂ H ₅ (15, 20), CH ₃ COC(A) ₂ C ₂ H ₅	275, 278,
Methyl <i>n</i> -propyl ketone	[C ₂ H ₅ CH ₂ N(CH ₃) ₃]OH; quaternized polyvinyl- pyridine resin	(14, 43), and ACH ₂ COC(A) ₂ C ₂ H ₅	478, 701

Methyl isopropyl ketone	KOH, C_2H_5OH ; [$C_4H_9CH_2N(CH_3)_2$]OH	$CH_3COC(A)(CH_3)_2$ (54)†	275
Diethyl ketone	[$C_4H_9CH_2N(CH_3)_2$]OH	$CH_3CH(A)COC(A)_2CH_3$ (31)	761
Methyl isobutyl ketone	KOH, C_2H_5OH ; [$C_4H_9CH_2N(CH_3)_2$]OH	$CH_3COC(A)(CH_3)_2$ (17) and $CH_3COC(A)_2CH(CH_3)_2$ (15)†	275, 701
Mesityl oxide	[$C_4H_9CH_2N(CH_3)_2$]OH	$CH_3COC(A)_2C(CH_3)=CH_2$ (35, 74) and $CH_3COC(A)=C(CH_3)_2$ (10-15)	764, 293
Methyl n amyl ketone	KOH, C_4H_9OH ; [$C_4H_9CH_2N(CH_3)_2$]OH	$CH_3COC(A)(C_4H_9)_n$ (19) and $CH_3COC(A)_2C_4H_9$ -n (40)†	275, 761
Diisopropyl ketone	[$C_4H_9CH_2N(CH_3)_2$]OH	$(CH_3)_2C(A)COC(A)(CH_3)_2$ (40, 10) and $(CH_3)_2C(A)COC(A)(CH_3)_2$ (1)†	274, 275, 785
	Aq. NaOH	$(CH_3)_2C(A)COC(A)(CH_3)_2$ (28) and $(CH_3)_2C(A)COC(A)_2(CH_3)_2$ (small)	788
Methyl hexyl ketone	[$C_4H_9CH_2N(CH_3)_2$]OH; KOH, C_2H_5OH	$CH_3COC(A)(C_4H_9)_n$ (19) and $CH_3COC(A)_2C_4H_9$ -n (31)†	275, 761
Diisobutyl ketone	KOH, C_4H_9OH ; [$C_4H_9CH_2N(CH_3)_2$]OH	$(CH_3)_2CHCH(A)COC(A)CH(CH_3)_2$ (35) and $(CH_3)_2CHCH(A)COC(A)(CH_3)_2$ (19)†	275
Isopropyl n-amyl ketone	KOH, CH_3OH	n- $C_5H_{11}COC(A)(CH_3)_2$	276
Isopropyl n-nonyl ketone	KOH, CH_3OH	n- $C_9H_{19}COC(A)(CH_3)_2$	276
Acetylacetone	[$C_4H_9CH_2N(CH_3)_2$]OH or OC_4H_9 -n	$CH_3COC(A)_2COC(A)_2$ (49-55)	277
Acetonylacetone	[$C_4H_9CH_2N(CH_3)_2$]OH or OC_4H_9 -n	$CH_3COC(A)_2CH_3COC(A)_2$ (46-50)	277
Cyclopentanone	[$C_4H_9CH_2N(CH_3)_2$]OH; KOH	2,2,5,5-Tetra-(β-cyanoethyl)cyclopentanone (97)	761
	[$C_4H_9CH_2N(CH_3)_2$]OH; [$C_4H_9N(CH_3)_2$]OC ₂ H ₅	2,2,5,5-Tetra-(β-cyanoethyl)cyclopentanone (95-97)	767

Note: References 491-1015 are on pp. 545-555.

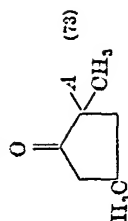
* Compare the review by Bruson.¹⁷⁴

† A large excess of the ketone was used in this experiment.

‡ The acrylonitrile was formed *in situ* from β-chloropropionitrile in the experiments described in ref. 275.

TABLE X—Continued

MICHAEL CONDENSATIONS WITH ACRYLONITRILE*		
Reactants	Catalyst	Product (Yield, %)
<i>C. Ketones (Cont.)</i>		$A = -CH_2CH_2CN$
Cyclohexanone	KOH, C_2H_5OH ; [$C_6H_5CH_2N(CH_3)_3$]OH [$C_6H_5CH_2N(CH_3)_3$]OH	2-(β -Cyanoethyl)cyclohexanone (16-19) and 2,2-di-(β -cyanoethyl)cyclohexanone (44)†
	NaNH ₂ Na; [$C_6H_5CH_2N(CH_3)_3$]OH; KOH NaOH	2-(β -Cyanoethyl)cyclohexanone (47) or 2,2-di-(β -cyanoethyl)cyclohexanone (18-20) 2,2,6,6-Tetra-(β -cyanoethyl)cyclohexanone (12)§ 2,2,6,6-Tetra-(β -cyanoethyl)cyclohexanone (81, 80-95)
	Enamine of the ketone with pyrrolidine $NaOC_2H_5$	2-(β -Cyanoethyl)cyclohexanone (20) and 2,2-Di-(β -cyanoethyl)cyclohexanone (40) 2-(β -Cyanoethyl)cyclohexanone (80)
	KOH	2-(β -Cyanoethyl)cyclohexanone (5), 2,2-di-(β -cyanoethyl)cyclohexanone (5), and 2,2,6,6-tetra-(β -cyanoethyl)cyclohexanone
	NaOCH ₃	2-(β -Cyanoethyl)cyclohexanone (29) and 2,2-di-(β -cyanoethyl)cyclohexanone (26) 2-(β -Cyanoethyl)cyclohexane-1,3-dione (23)

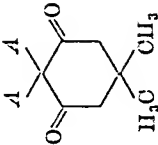
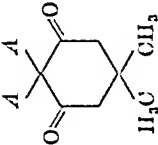
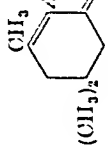
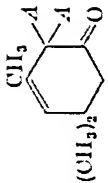
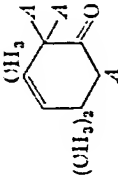



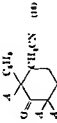
2,4-Dimethylcyclopentan-1-one

KOH

709

TABLE X—Continued

MICHAEL CONDENSATIONS WITH ACRYLONITRILE*			References
Reactants	Catalyst	Product (Yield, %) $A = -CH_2CH_2CN$	
<i>C. Ketones (Cont.)</i>			
5,5-Dimethylcyclohexano-1,3-dione (Cont.)	$NaOC_2H_5$	 (83) **	234
	$NaNH_2$	 §	234
Isophorone	$[C_6H_6CH_2N(CH_3)_3]OH$	 †† (9)	295
		 (22)	
		 (1)	

4,4-Amylcyclohexanone	NaOC_4H_9 ^d		286
2-(Cyclohex-1'-enyl)cyclohexanone	$[\text{C}_6\text{H}_9\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH};$ KOH	2,2,6,6-Tetra-(β-cyanoethyl)-4-amylocyclohexanone (80-95)	761
4-Cyclohexylcyclohexanone	$[\text{C}_6\text{H}_9\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	2-Cyclohex-1'-enyl-2-(β-cyanoethyl)cyclohexanone (50) and 2-cyclohex-1-enyl-2,6,6-tri(β-cyanoethyl)cyclohexanone (29)	279
3-Oxo-2-phenylcyclohexyl-acetonitrile	$[\text{C}_6\text{H}_9\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH};$ KOH	2,2,6,6-Tetra-(β-cyanoethyl)-4-cyclohexylcyclohexanone (80-95)	701
	$[\text{C}_6\text{H}_9\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$		104

Note: References 491-1015 are on pp. 545-555.

^a Compare the review by Bruson.⁴¹

[†] The acrylonitrile was formed *in situ* from the methiodide of 2-diethylaminopropionitrile.

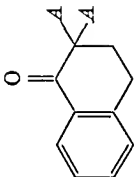
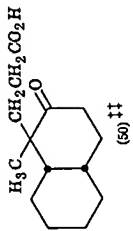
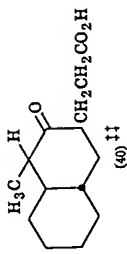
^{**} The diketone was recovered to an extent of 31%. When β-chloropropionitrile was employed instead of acrylonitrile, the yield was 21%, and 52% of the diketone was recovered.

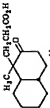


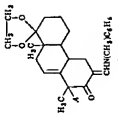
^{††} This structure has been proven (ref. 286) by ozonization to 3,3-dimethyl-5-oxohexano-1-carboxylic acid. In ref. 285, the isomeric formula



was incorrectly assigned to the monosubstitution product.

TABLE X—Continued

MICHAEL CONDENSATIONS WITH ACRYLONITRILE*			References
Reactants	Catalyst	Product (Yield, %)	
<i>C. Kelones (Cont.)</i>		$A = -CH_2CH_2CN$	
2-Phenylcyclohexanone	$NaNH_2$ $[C_6H_5CH_2N(CH_3)_3]OH$	2-(β -Cyanoethyl)-2-phenylcyclohexanone (63-70)	112
	Na	2-(β -Cyanoethyl)-2-phenylcyclohexanone (80)	113
	$[C_6H_5CH_2N(CH_3)_3]OH$	2-(β -Cyanoethyl)-2-phenylcyclohexanone (80)	773
4-($\alpha,\alpha,\gamma,\gamma$ -Tetramethylbutyl)-cyclohexanone	$[C_6H_5CH_2N(CH_3)_3]OH$	2,2,6,6-Tetra-(β -cyanoethyl)-4-($\alpha,\alpha,\gamma,\gamma$ -tetramethylbutyl)cyclohexanone (80-95)	761
2-Benzylidene-6-phenylcyclohexanone	$[C_6H_5CH_2N(CH_3)_3]OH$	2-Benzylidene-6-(β -cyanoethyl)-6-phenylcyclohexanone (83)	112
α -Tetralone	$[C_6H_5CH_2N(CH_3)_3]OH$; KOH		761
1-Methyl-cis-2-decalone	$[C_6H_5CH_2N(CH_3)_3]OH$	 (50) ††	368
1-Methyl- <i>trans</i> -2-decalone	$[C_6H_5CH_2N(CH_3)_3]OH$	 (40) ††	368

3-(Methylanulomethylene)-1-methyl-4- <i>trans</i> -2-decalone	$[C_4H_9CH_2N(CH_3)_2]OH$		308
	$[C_4H_9CH_2N(CH_3)_2]OH$		108
	$[C_4H_9CH_2N(CH_3)_2]OH$		108
	$[C_4H_9CH_2N(CH_3)_2]OH$		542

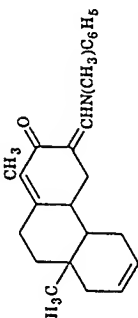
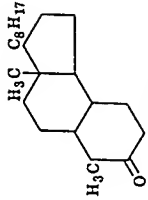
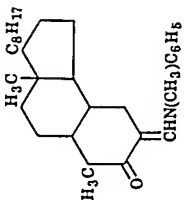
Note: References 491-1045 are on pp. 545-553.

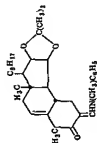
* Compare the review by Brunson.¹¹⁴

†† This product was isolated after saponification of the adduct.

TABLE X—Continued

MICHAEL CONDENSATIONS WITH ACRYLONITRILE*

Reactants	Catalyst	Product (Yield, %)	References
<p><i>C. Kclones (Cont.)</i></p> 			
 <p>(Inhoffen ketone)</p>	$[\text{C}_6\text{H}_5\text{N}(\text{CH}_3)_3]\text{OH}$		774
	$[\text{C}_6\text{H}_5\text{N}(\text{CH}_3)_3]\text{OH}$		368
			368, 775



Acetophenone

4-Chloroacetophenone

4-Bromoacetophenone

4-Methylacetophenone

4-Methoxyacetophenone

Propiophenone

Phenylacetone

 $[\text{C}_6\text{H}_5\text{N}(\text{CH}_3)_3]\text{OH}$ $[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$
or $\text{OC}_6\text{H}_5^{\text{m}}$

Aq. KCN

 $[\text{C}_6\text{H}_5\text{N}(\text{CH}_3)_3]\text{OC}_6\text{H}_5$ $[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]^{\text{p}}$ $\text{OC}_6\text{H}_5^{\text{m}}$ $[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$ $[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH};$

KOH

 $[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH};$

KOH

 $[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH};$

KOH

 $[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH};$

KOH

 $[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH};$

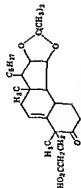
KOH

 $[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH};$

KOH

Na enolate

Note: References 491-1095 are on pp. 545-555.

* Compare the review by Bruson.²⁷⁴(35% α and 65% β isomer) $\text{C}_6\text{H}_5\text{COC}(\text{A})_3$ (57-64) $\text{C}_6\text{H}_5\text{COCH}(\text{A})_3$ (36) and $\text{C}_6\text{H}_5\text{COC}(\text{A})_3$ (small) $\text{C}_6\text{H}_5\text{COC}(\text{A})_3$ (85) $\text{C}_6\text{H}_5\text{COC}(\text{A})_3$ (84) $\text{C}_6\text{H}_5\text{COC}(\text{A})_3$ (57) $p\text{-ClC}_6\text{H}_4\text{COC}(\text{A})_3$ $p\text{-BrC}_6\text{H}_4\text{COC}(\text{A})_3$ $p\text{-CH}_3\text{C}_6\text{H}_4\text{COC}(\text{A})_3$ $p\text{-CH}_3\text{OC}_6\text{H}_4\text{COC}(\text{A})_3$ $\text{C}_6\text{H}_5\text{COC}(\text{A})_3\text{CH}_3$ (quant.) $\text{C}_6\text{H}_5\text{C}(\text{A})_3\text{COCH}_3$ (86) $\text{C}_6\text{H}_5\text{CH}(\text{A})_3\text{COCH}_3$ (80)

551

277, 279,

761

776

767

767

767

761

761

761

761

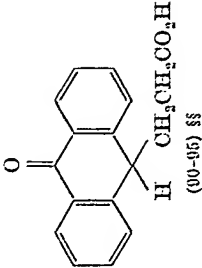
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



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761

107

TABLE X—Continued
MICHAEL CONDENSATIONS WITH ACRYLONITRILE*

Reactants	Catalyst	Product (Yield, %)	References
<i>C. Ketones (Cont.)</i>			
Isobutyrophenone	KOH, CH ₃ OH	C ₆ H ₅ COC(A)(CH ₃) ₃	276
Benzoylacetone	[C ₆ H ₅ CH ₂ N(CH ₃) ₃]OH or OC ₄ H ₉ - <i>n</i>	C ₆ H ₅ COC(A) ₂ COCH ₃	277
2,4,6-Trimethylacetophenone	[C ₆ H ₃ CH ₂ N(CH ₃) ₃]OH; KOH	2,4,6-(CH ₃) ₃ C ₆ H ₂ COC(A) ₃ (30)	761
Isopropyl benzyl ketone	KOH, CH ₃ OH	C ₆ H ₅ CH ₂ COC(A)(CH ₃) ₃	276
Methyl β-naphthyl ketone	[C ₆ H ₅ CH ₂ N(CH ₃) ₃]OH	β-C ₁₀ H ₇ COC(A) ₃	761
α- <i>n</i> -Butylpropiofenone	KOH, CH ₃ OH	C ₆ H ₅ COC(A)(CH ₃)C ₄ H ₉ - <i>n</i>	276
α- <i>n</i> -Propylbutyrophenone	KOH, CH ₃ OH	C ₆ H ₅ COC(A)(C ₃ H ₇)C ₃ H ₇ - <i>n</i>	276
Deoxybenzoin	[C ₆ H ₅ CH ₂ N(CH ₃) ₃]OH; KOH	C ₆ H ₅ C(A) ₂ COC ₂ H ₅ (80)	761
Anthrone	[C ₆ H ₅ CH ₂ N(CH ₃) ₃]OH	9,9-Di-(β-cyanoethyl)-10-anthrone (89)	288
	KOC ₄ H ₉ - <i>t</i>		777
4-Phenylacetophenone	[C ₆ H ₅ CH ₂ N(CH ₃) ₃]OH; KOH	4-C ₆ H ₅ C ₆ H ₄ COC(A) ₃	701
Dibenzyl ketone	[C ₆ H ₅ CH ₂ N(CH ₃) ₃]OH; KOH	C ₆ H ₅ C(A) ₂ COCH(A)C ₆ H ₅	761


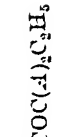






α -n-Octylpropiofenone	KOH, CH_3OH	$\text{C}_8\text{H}_{17}\text{COC(A)}(\text{CH}_3)_2\text{C}_8\text{H}_{17-n}$	276
Methyl α -phenylmethyl ketone	KOH, CH_3OH	$\text{CH}_3\text{COC(A)}(\text{C}_6\text{H}_5) \text{C}_6\text{H}_5$	276
2-Acetylfuran	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$ or OC_6H_5-n	 COC(A)_2 (90-93)	277, 279
2-Acetyl-5-methylfuran	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	 COC(A)_2 (71)	778
2-Propionylfuran	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	 $\text{COC(A)}_2\text{CH}_3$ (Quast)	279
3-Acetyl-2,5-dimethylfuran	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	 COC(A)_2 (16)	778
2-Propionyl-5-methylfuran	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	 $\text{COC(A)}_2\text{CH}_3$ (62)	778
2-n-Butylfuran	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	 $\text{COC(A)}_2\text{CH}_2\text{CH}_3$ (70)	279
2,5-Dimethyl-3-propionylfuran	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	 $\text{COC(A)}_2\text{CH}_3$ (27)	778

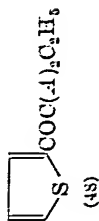
Note: References 401-1045 are on pp. 543-553.


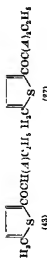
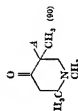
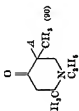
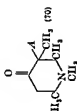
* Compare the review by Brunson.²⁷⁴

† Arylnitrile was formed *in situ* from β -chloropropionitrile.

TABLE X—Continued
MICHAEL CONDENSATIONS WITH ACRYLONITRILE*

Reactants	Catalyst	Product (Yield, %)	References
<i>C. Keflones (Cont.)</i>			
2- <i>n</i> -Butyryl-5-methylfuran	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	H_3C  (53) $\text{COC}(\text{A})\text{C}_2\text{H}_5$  (47)	778
3- <i>n</i> -Butyryl-2,5-dimethylfuran	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	$\text{COC}(\text{A})\text{C}_2\text{H}_5$  (54)	778
2-Acetylthiophene	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$ or OC_4H_9 ⁿ	 (57-80)	277, 279
2-Acetyl-5-methylthiophene	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	 (80)	778
2-Propionylthiophene	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	 (98)	279
5-Methyl-2-propionylthiophene	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	 (70)	778
2- <i>n</i> -Butyrylthiophene	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	 (30)	778



2-Acetoxyacetylthiophene	$[\text{C}_4\text{H}_4\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$		(40)	277
5-Methyl-2-n-butylthiophene	$[\text{C}_4\text{H}_4\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$		(43)	778
1,2,5-Trimethyl-4-piperidone	KOH		(90)	769
2,5-Dimethyl-1-ethyl-4-piperidone	KOH		(90)	769
1,2,3,6-Tetramethyl-4-piperidone	KOH		(70)	769

Note: References 491-1015 are on pp. 545-555.

* Compare the review by Bruson.¹⁷¹

TABLE X—Continued
MICHAEL CONDENSATIONS WITH ACRYLONITRILE*

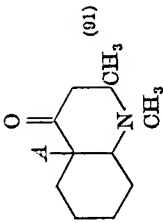
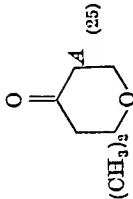
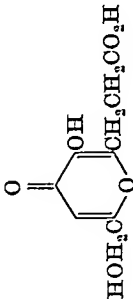

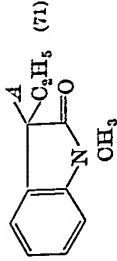
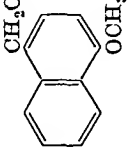
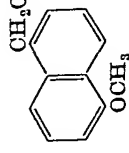


Reactants	Catalyst	Product (Yield, %)	References
<i>C. Ketones (Cont.)</i>		<i>A</i> = —CH ₂ CH ₂ CN	
1,2-Dimethyloctahydro-4-(1H)-quinolone	KOH	 (91)	769
2,2-Dimethyl-4-pyrone	KOH	 (25)	769
Kojic acid	[C ₆ H ₅ CH ₂ N(CH ₃) ₃]OH	 (47)	170
3-Oxo-2,2,5,5-tetramethyltetrahydrofuran	[C ₆ H ₅ CH ₂ N(CH ₃) ₃]OH; KOH	 (63)	761
3-Ethyl-1-methylloxindole	[C ₆ H ₅ CH ₂ N(CH ₃) ₃]OH	 (71)	779

TABLE X—Continued
MICHAEL CONDENSATIONS WITH ACRYLONITRILE*

Reactants	Catalyst	Product (Yield, %)	References
<i>D. Esters and Amides (Cont.)</i>		$A = -CH_2CH_2CN$	
Diethyl 2-naphthylmalonate	KOH, CH_3OH	α -(2-Naphthyl)glutaric acid††	783
Diethyl (1-naphthylmethyl)-malonate	KOH, CH_3OH	α -(1-Naphthylmethyl)glutaric acid††	783
Diethyl (2-naphthylmethyl)-malonate	KOH, CH_3OH	α -(2-Naphthylmethyl)glutaric acid††	783
Diethyl (β -1-naphthylethyl)-malonate	KOH, CH_3OH	α -(β -1-Naphthylethyl)glutaric acid††	783
Diethyl (β -2-naphthylethyl)-malonate	KOH, CH_3OH	α -(β -2-Naphthylethyl)glutaric acid††	783
Vinylacetamide (or crotonamide)	$[C_6H_5CH_2N(CH_3)_3]OH$	$CH_2=CHC(A)_2CONH_2$ (18)	283
Diethyl β -(4-methoxy-1-naphthyl)ethylmalonate	KOH, CH_3OH , (CH_3) ₃ COH	 $CH_2CH_2CHCO_2H$ †† $ $ $CH_2CH_2CO_2H$ (40)	786
Diethyl β -(6-methoxy-1-naphthyl)ethylmalonate	KOH, CH_3OH , (CH_3) ₃ COH	 $CH_2CH_2CHCO_2H$ †† $ $ $CH_2CH_2CO_2H$ (32)	786


• Diethyl β -(6-methoxy-1-naphthyl)ethylmalonate	KOH, CH ₃ OH, (CH ₃) ₂ COH		CH ₃ CH ₂ CH(CO ₂ H) \ddagger CH ₂ CH ₂ C ¹⁸ O ₂ H (61)	786
Diethyl β -(7-methoxy-1-naphthyl)ethylmalonate	KOH, CH ₃ OH, (CH ₃) ₂ COH		CH ₃ CH ₂ CH(CO ₂ H) \ddagger CH ₂ CH ₂ CO ₂ H	786
Diethyl formamidomalonate	NaOC ₂ H ₅		Glutamic acid $\ddagger\ddagger$ (55)	459
Diethyl acetamidomalonate	NaOC ₂ H ₅		CH ₃ CONH(C(A)(CO ₂ C ₂ H ₅) ₂) ₂ (65)	458
Ethyl cyanoacetate	Aq. NaOH		NCC(A)(CO ₂ C ₂ H ₅) ₂ , NCC(A) ₂ CO ₂ C ₂ H ₅	469
	[C ₂ H ₅ CH ₂ N(CH ₃) ₂]OH NaCN		NCC(A) ₂ CO ₂ C ₂ H ₅ (quant.)	307, 282
Cyanoacetamide	[C ₂ H ₅ CH ₂ N(CH ₃) ₂]OH		NCC(A)(CO ₂ C ₂ H ₅) ₂ and a little NCC(A) ₂ CO ₂ C ₂ H ₅	469
Ethyl α -isopropylcyanoacetate	KOH, CH ₃ OH		NCC(A) ₂ CONH ₂ (50)	282
Diethyl α -methyl- α' -cyano-succinate	NaOCH ₃		α -isopropylglutaric acid $\ddagger\ddagger$	783
Ethyl α,β -dicyano- β -methyl-butyrate	[C ₂ H ₅ CH ₂ N(CH ₃) ₂]OH		C ₂ H ₅ O ₂ CCH(CH ₃)C(CN)(A)CO ₂ C ₂ H ₅ (91)	787
Diethyl α -cyano- β,β -dimethyl-glutarate	Not indicated		(CH ₃) ₂ C(CN)C(A)(CN)CO ₂ C ₂ H ₅ (89)	788, 789
Diethyl 3,4-dicyano-3-methyl-butane-1,4-dicarboxylate	[C ₂ H ₅ CH ₂ N(CH ₃) ₂]OH		C ₂ H ₅ O ₂ CCH ₂ C(CH ₃) ₂ C(A)(CN)CO ₂ C ₂ H ₅ (72)	790
			4C(CN)(CO ₂ C ₂ H ₅)C(CN)(CH ₃)CH ₂ CH ₂ CO ₂ C ₂ H ₅ (83)	791

Note: References 491-1045 are on pp. 545-555.

* Compare the review by Bruson.¹¹⁶



$\ddagger\ddagger$ This product was isolated after saponification of the adduct.

TABLE X—Continued

MICHAEL CONDENSATIONS WITH ACRYLONITRILE*		
Reactants	Catalyst	Product (Yield, %)
		$A = -CH_2CH_2CN$
<i>D. Esters and Amides (Cont.)</i>		
Ethyl phenylethanoacetate	KOH, CH_3OH	$C_6H_5C(A)(CN)(CO_2C_2H_5)$ (89–83)
Diethyl 1,2-dicyano-2-methylpentane-1,5-dicarboxylate	$[C_6H_5CH_2N(CH_3)_3]OH$	$C_2H_5O_2C(CH_2)_3C(CN)(CH_3)C(A)(CN)CO_2C_2H_5$ (99)
Methyl ethylphenylacetate	$NaOCH_3$	$(C_6H_5)(C_2H_5)C(A)CO_2CH_3$
Methyl <i>n</i> -propylphenylacetate	$NaOCH_3$	$(C_6H_5)(n-C_3H_7)C(A)CO_2CH_3$
Methyl <i>n</i> -butylphenylacetate	$NaOCH_3$	$(C_6H_5)(n-C_4H_9)C(A)CO_2CH_3$
Methyl isobutylphenylacetate	$NaOCH_3$	$C_6H_5(i-C_4H_9)C(A)CO_2CH_3$
Methyl diphenylacetate	$NaOCH_3$	$(C_6H_5)_2C(A)CO_2CH_3$
Methyl fluorene-9-carboxylate	KOH	9-Carbomethoxy-9-(β -cyanoethyl)fluorene (94)
Ethyl 1-methylfluorene-9-carboxylate	NaOH, pyridine	9-Carbomethoxy-9-(β -cyanoethyl)-1-methylfluorene (78)
Ethyl 2,7-dibromofluorene-9-carboxylate	$[C_6H_5CH_2N(CH_3)_3]OH$	9-Carbomethoxy-9-(β -cyanoethyl)-2,7-dibromofluorene (93)
Methyl 4-cyclopenta[def]-phenanthrene-4-carboxylate	$[C_6H_5CH_2N(CH_3)_3]OH$	
Ethyl α -furylacetate	$[C_6H_5CH_2N(CH_3)_3]OH$ or OC_4H_9-n	 (90)

797

277

Ethyl α -thienylacetate	$[C_4H_5CH_2N(CH_3)_2]OH$ or $OC_4H_5 \cdot n$	 (32)	277
Ethyl 2-pyridylacetate	Na	 (72)	798
<i>E. Keto Esters and Amides</i>			
Methyl acetoacetate	$[C_4H_5CH_2N(CH_3)_2]OH$	$CH_3COC(A)_2CO_2CH_3$ (49)	760, 761
Ethyl acetoacetate	$[C_4H_5CH_2N(CH_3)_2]OH$ or $OC_4H_5 \cdot n$	$CH_3COC(A)_2CO_2C_2H_5$ (79-80) or $CH_3COCH(A)CO_2C_2H_5$ (79-80)	277, 760, 761, 767
	$[C_4H_5CH_2N(CH_3)_2]OC_2H_5$	$CH_3COC(A)_2CO_2C_2H_5$ (83)	767
	$NaOC_2H_5$	$CH_3COC(A)_2CO_2C_2H_5$ (40)	799
Ethyl methylacetoacetate	$KOH, CH_3OH,$ $(CH_3)_3COH$	$CH_3COC(CH_3)(A)CO_2C_2H_5$ (58, 57)	766, 800
	$NaOC_2H_5$	α -Methylglutaric acid (51)††	800
	—	$CH_3COC(CH_3)(A)CO_2C_2H_5$ (61)	782
Ethyl ethylacetoacetate	$KOH, CH_3OH,$ $(CH_3)_3COH$	$CH_3COCH(A)CH_2$ (34)††	801
	—	$CH_3COC(C_2H_5)(A)CO_2C_2H_5$ (62)	800
	—	α -Ethylglutaric acid (62)††	800
Ethyl n-propylacetoacetate	$KOH, CH_3OH,$ $(CH_3)_3COH$	$CH_3COCH(A)CH_2CH_3$ (43)††	801
	—	$CH_3COC(C_2H_5)(A)CO_2C_2H_5$ (88)	800
	—	α -n-Propylglutaric acid (88)††	800
	—	$CH_3COCH(A)CH_2CH_2CH_3$ (36)††	801




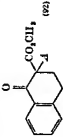
Note: References 491-1045 are on pp. 545-555.

* Compare the review by Bruson.¹¹⁴

†† This product was isolated after saponification of the adduct.

TABLE X—Continued
MICHAEL CONDENSATIONS WITH ACRYLONITRILE*

Reactants	Catalyst	Product (Yield, %)	References
<i>E. Kelo Esters and Amides (Cont.)</i>		$A = -CH_2CH_2CN$	
Ethyl isopropylacetate	KOH, CH_3OH , $(CH_3)_3COH$	$CH_3COC(C_3H_7-i)(A)CO_2C_2H_5$ (37, 43)	591, 800
Ethyl allylacetate	KOH, CH_3OH , $(CH_3)_3COH$	α -Isopropylglutaric acid (43)†† $CH_3COC(C_3H_7)(A)CO_2C_2H_5$ (76)	800 800
Ethyl <i>n</i> -butylacetate	KOH, CH_3OH , $(CH_3)_3COH$	α -Allylglutaric acid (76)†† $CH_3COC(C_4H_9-n)(A)CO_2C_2H_5$ (74–75)	119, 800 800
Ethyl <i>n</i> -amylacetate	— KOH, CH_3OH , $(CH_3)_3COH$; Na	α - <i>n</i> -Butylglutaric acid (75)†† $CH_3COCH(A)CH_2CH_2CH_2CH_3$ (35)†† $CH_3COC(C_5H_{11}-n)(A)CO_2C_2H_5$ (71)	801 781, 800
Ethyl isoamylacetate	— KOH, CH_3OH , $(CH_3)_3COH$	α - <i>n</i> -Amylglutaric acid (71)†† $CH_3COCH(A)(CH_2)_4CH_3$ (32)††	800 801
Ethyl <i>n</i> -hexylacetate	KOH, CH_3OH , $(CH_3)_3COH$	$CH_3COC(C_6H_{11}-i)(A)CO_2C_2H_5$ (72)	800
Ethyl phenylacetate	KOH, CH_3OH , $(CH_3)_3COH$	α -Isoamylglutaric acid (72)†† $CH_3COC(C_6H_{13}-n)(A)CO_2C_2H_5$ (84)	800 800
Ethyl benzylacetate	$NaOC_2H_5$; KOH, CH_3OH , $(CH_3)_3COH$	α - <i>n</i> -Hexylglutaric acid (84)†† $CH_3COC(C_6H_5)(A)CO_2C_2H_5$ (27)	800 802
Ethyl <i>n</i> -butylacetate	— $[C_6H_5CH_2N(CH_3)_3]OH$ or OC_4H_9-n $NaOC_2H_5$	$CH_3COC(CH_2C_6H_5)(A)CO_2C_2H_5$ (85) $CH_3COC(CH_2C_6H_5)(A)CO_2C_2H_5$ (66) α -Benzylglutaric acid (66)†† $CH_3COCH(A)CH_2C_6H_5$ (31)†† $n-C_3H_7COC(A)_2CO_2C_2H_5$ (34–36, 74) $n-C_3H_7COCH(A)CO_2C_2H_5$ (52)	581 800 800 801 217, 119 799

Ethyl isobutyrylacetate	$[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$ or $\text{OC}_2\text{H}_5^{\text{m}}$	$(\text{CH}_3)_3\text{CHCOC}(\text{A})_2\text{CO}_2\text{C}_2\text{H}_5$ (65-68)	277
Ethyl isobutyrylacetate	NaOC_2H_5	$(\text{CH}_3)_3\text{CHCOC}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (53)	799
Ethyl hexanoylacetate	NaOC_2H_5	$n\text{-C}_6\text{H}_{13}\text{COC}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (46)	799
Ethyl hexanoylacetate	NaOC_2H_5	$n\text{-C}_6\text{H}_{13}\text{COC}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (38, 67)	799, 803
Ethyl heptanoylacetate	NaOC_2H_5	$n\text{-C}_7\text{H}_{15}\text{COC}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (35)	799
Ethyl benzoylacetate	$[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$ or $\text{OC}_2\text{H}_5^{\text{m}}$	$\text{C}_6\text{H}_5\text{COC}(\text{A})_2\text{CO}_2\text{C}_2\text{H}_5$ (53)	277
	NaOC_2H_5	$\text{C}_6\text{H}_5\text{COC}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (86, 43)	581, 799
Ethyl 2-furylacetate	NaOC_2H_5	 $\text{COCH}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (37)	799
Ethyl 2-thienylacetate	NaOC_2H_5	 $\text{COCH}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (44)	799
2-Carboxycyclohexanone	$\text{KOH}, \text{C}_2\text{H}_5\text{OH};$ $\text{NaOC}_2\text{H}_5; \text{NaNH}_2;$ $[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	 $\text{CO}_2\text{C}_2\text{H}_5$ (85)	119, 121, 694
Methyl camphor-3-carboxylate	$\text{KOH}, \text{C}_2\text{H}_5\text{OH}$	3-Carboxymethoxy-3-(β-cyanoethyl)camphor (78)	119
2-Carboxymethoxy-1-tetralone	$[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	 CO_2CH_2 (92)	804





Note: References 491-1015 are on pp. 615-655.

* Compare this review by Iruwan.¹⁰⁴

** This product was isolated after saponification of the adduct.

TABLE X—Continued

MICHAEL CONDENSATIONS WITH ACRYLONITRILE*			References
Reactants	Catalyst	Product (Yield, %)	
<i>E. Keto Esters and Amides (Cont.)</i>			
Acetoacetalanilide	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	$\text{CH}_3\text{COC}(\text{A})_2\text{CONHC}_6\text{H}_5$	760
Acetoacet-2-chloroanilide	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	$\text{CH}_3\text{COC}(\text{A})_2\text{CONHC}_6\text{H}_4\text{Cl-o}$	700
Acetoacet-2,5-dichloroanilide	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	$\text{CH}_3\text{COC}(\text{A})_2\text{CONHC}_6\text{H}_3\text{Cl}_2\text{-2,5}$	760
Acetobutyrolactone	NaOC_2H_5	2-Aceto-2-(β -cyanoethyl)butyrolactone (80-92)	581
<i>F. Nitriles</i>			
Allyl cyanide (or crotononitrile)	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	$\text{CH}_3\text{CH}=\text{C}(\text{A})\text{CN}$ (9)	283
Isopropenyl cyanide (or β , β -dimethylacrylonitrile)	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	$\text{CH}_2=\text{CHC}(\text{A})_2\text{CN}$ (23)	283
Benzyl cyanide	Aq. NaCN	$(\text{CH}_3)_2\text{C}=\text{C}(\text{A})\text{CN}$ (5)	460
	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	$\text{C}_6\text{H}_5\text{CH}(\text{A})\text{CN}$ (80)	282
	NaOC_2H_5	$\text{C}_6\text{H}_5\text{C}(\text{A})_2\text{CN}$ (94)	805
	$\text{KOH}, \text{CH}_3\text{OH}, (\text{CH}_3)_3\text{COH}$	$\text{C}_6\text{H}_5\text{C}(\text{A})_2\text{CN}$ (46)	767
	$[\text{C}_6\text{H}_5\text{N}(\text{CH}_3)_3]\text{OC}_2\text{H}_5$	$\text{C}_6\text{H}_5\text{C}(\text{A})_2\text{CN}$ (70)	767
	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	$\text{C}_6\text{H}_5\text{C}(\text{A})_2\text{CN}$ (90)	282
	$\text{KOH}, \text{CH}_3\text{OH}, (\text{CH}_3)_3\text{COH}$	$p\text{-O}_2\text{NC}_6\text{H}_4\text{C}(\text{A})_2\text{CN}$ (90)	809
	$\text{KOH}, \text{CH}_3\text{OH}, (\text{CH}_3)_3\text{COH}$	$o\text{-ClC}_6\text{H}_4\text{C}(\text{A})_2\text{CN}$ (47)	800
	KOH	$m\text{-ClC}_6\text{H}_4\text{C}(\text{A})_2\text{CN}$ (64)	807
<i>p</i> -Nitrobenzyl cyanide	$\text{KOH}, \text{CH}_3\text{OH}, (\text{CH}_3)_3\text{COH}$	$p\text{-ClC}_6\text{H}_4\text{C}(\text{A})_2\text{CN}$ (80)	806
<i>o</i> -Chlorobenzyl cyanide	$\text{KOH}, \text{CH}_3\text{OH}, (\text{CH}_3)_3\text{COH}$	$m\text{-BrC}_6\text{H}_4\text{C}(\text{A})_2\text{CN}$ (80)	806
<i>m</i> -Chlorobenzyl cyanide	$\text{KOH}, \text{CH}_3\text{OH}, (\text{CH}_3)_3\text{COH}$	$p\text{-BrC}_6\text{H}_4\text{C}(\text{A})_2\text{CN}$ (84)	806
<i>m</i> -Bromobenzyl cyanide	$\text{KOH}, \text{CH}_3\text{OH}, (\text{CH}_3)_3\text{COH}$	$m\text{-ClC}_6\text{H}_4\text{C}(\text{A})_2\text{CN}$ (88)	806
<i>p</i> -Bromobenzyl cyanide	$\text{KOH}, \text{CH}_3\text{OH}, (\text{CH}_3)_3\text{COH}$	$p\text{-CH}_3\text{C}_6\text{H}_4\text{C}(\text{A})_2\text{CN}$ (95)	806
<i>m</i> -Methylbenzyl cyanide	$\text{KOH}, \text{CH}_3\text{OH}, (\text{CH}_3)_3\text{COH}$	$(\text{C}_6\text{H}_5)(\text{CH}_3)\text{C}(\text{A})\text{CN}$ (55)	758
<i>p</i> -Methylbenzyl cyanide	$\text{KOH}, \text{CH}_3\text{OH}, (\text{CH}_3)_3\text{COH}$		
α -Phenylpropionitrile			

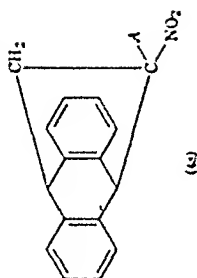
<i>p</i> -Isopropylbenzyl cyanide	KOH	$p\text{-(CH}_3)_2\text{CHC}_6\text{H}_4\text{C}(\Delta)_2\text{CN}$	807
Cyclohexenylacetonitrile	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$		283
α -(2-Thienyl)benzyl cyanide	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$		808
α -Naphthylacetonitrile	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	$\alpha\text{-C}_{10}\text{H}_7\text{C}(\Delta)_2\text{CN}$ (55)	807
α -(1-Cyclohexenyl)benzyl cyanide	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$		808
1-Cyano-2-benzoyl-1,2-dihydro-isoquinoline	Li salt		805a
<i>G. Nitro Compounds</i>			
Nitromethane	NaOCH_3 ; aq. K_2CO_3 $[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$ $(\text{C}_6\text{H}_5)_2\text{NH}$; NaOCH_3 Aq. K_2CO_3	$(\Delta)_2\text{CHNO}_2$ (low); $(\Delta)_2\text{CNO}_2$ (52) $(\Delta)_2\text{CNO}_2$ (45) $\text{CH}_2\text{CH}(\Delta)\text{NO}_2$ (30) $\text{CH}_2\text{C}(\Delta)_2\text{NO}_2$ (87) $(\text{CH}_3)_2\text{C}(\Delta)\text{NO}_2$ (78)	117, 281 282 117, 280 281
2-Nitropropane	Aq. KOH	1-Nitro-1-(β -cyanoethyl)cyclohexane (40)	117
Nitrocyclohexane	Aq. KOH	$(\Delta)_2\text{C}(\text{NO}_2)_2$ (34); $(\Delta)_2\text{CNO}_2$ (12)	117
$\text{O}_2\text{NCH}=\text{NO}_2\text{K}$	Aq. solution		809

Note: References 491-1045 are on pp. 545-555.

* Compare the review by Druson.⁷⁴

TABLE X—Continued

MICHAEL CONDENSATIONS WITH ACRYLONITRILE*			
Reactants	Catalyst	Product (Yield, %)	References
<i>G. Nitro Compounds (Cont.)</i>		$A = -CH_2CH_2CN$	
$CH_3O_2CCH_2CH_2C(NO_2)=NO_2Na$	Aq. solution	$A C(NO_2)_2CH_2CH_2CO_2CH_3$	S10
<i>p</i> -Bromophenylnitromethane	$[C_6H_5CH_2N(CH_3)_3]OH$	$p\text{-}BrC_6H_4C(A)N_2NO_2$ (15)	117
Methyl 2-nitro-1-phenylpropyl ether	Aq. NaOH	3-Nitro-3-methyl-4-methoxy-4-phenylvaleronitrile (30)	117
<i>n</i> -Butyl 3-nitro- <i>n</i> -butyl sulfone	$[CH_3N(C_2H_5)_3]OH$	3-Nitro-3-methyl-5-(butylsulfonyl)-1-pentanecarbonitrile	117
Ethyl nitroacetate	KOH, ethanol	Ethyl α -nitro- γ -cyanobutyrate (10)	S11
	$[C_2H_5CH_2N(CH_3)_3]OH$	$O_2NCH(A)CO_2C_2H_5$ (52)	S12
	$(C_2H_5)_2NH$	$O_2NC(A)_2CO_2C_2H_5$ (80)	S12
	Na derivative in water	$O_2NCH(A)CO_2C_2H_5$ (diethylamine salt) (S1)	622
Methyl γ,γ -dinitrobutyrate		Methyl 6-cyano-1,4-dinitrohexanoate (51)	S10



Endo-(nitroethylene)anthracene

S13

H. Sulfones

Phenyl benzyl sulfone	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	$\text{C}_6\text{H}_5\text{SO}_2\text{C}(\text{A})_2\text{C}_2\text{H}_5$ (60)	279, 814
Allyl <i>p</i> -tolyl sulfone	$[\text{C}_6\text{H}_4\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{CH}(\text{A})\text{CH}=\text{CH}_2$ and $p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{A})_2\text{CH}=\text{CH}_2$	814
$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	$\text{KOH}, \text{CH}_3\text{OH}$	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{C}(\text{A})_2\text{CO}_2\text{C}_2\text{H}_5$	814
Phenyl <i>p</i> -chlorobenzyl sulfone ^{††}	$[\text{C}_6\text{H}_4\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	$p\text{-ClC}_6\text{H}_4\text{C}(\text{A})_2\text{SO}_2\text{C}_2\text{H}_5$ (60)	815

I. Phosphonacetates

Triethyl phosphonoacetate	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$ NaOC_2H_5	$(\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{O})\text{C}(\text{A})_2\text{CO}_2\text{C}_2\text{H}_5$ (87)	816
	Na	$(\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{O})\text{CH}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (28)	124
	K	$(\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{O})\text{C}(\text{A})_2\text{CO}_2\text{C}_2\text{H}_5$ (27)	817
Diethyl cyanomethanephosphonate [‡]	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	$(\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{O})\text{CH}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (40)	
	K	$(\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{O})\text{C}(\text{A})_2\text{CO}_2\text{C}_2\text{H}_5$ (19)	817
	K	$(\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{O})\text{C}(\text{A})_2\text{CO}_2\text{C}_2\text{H}_5$ (68)	810
	K	$(\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{O})\text{C}(\text{CN})(\text{A})_2$ (90)	
Triethyl α -phosphonopropionate	NaOC_2H_5	$(\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{O})\text{C}(\text{CN})(\text{A})_2$ (80)	817
Triethyl α -phosphonohexanoate	NaOC_2H_5 K	$(\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{O})\text{C}(\text{CH}_3)(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (58)	124
		$(\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{O})\text{C}(\text{C}_6\text{H}_5)(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (71)	124
		$(\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{O})\text{C}(\text{C}_6\text{H}_5)(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (73)	817

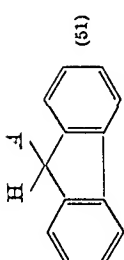
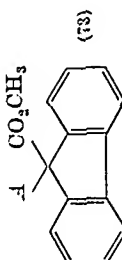
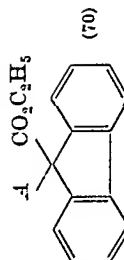
Note: References 491-1015 are on pp. 545-555.


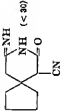

* Compare the review by Bruson.^{27a}

^{††} The ortho and meta isomers gave analogous reactions, only the para isomer failed to react.

From *o*- and *m*-methyl benzylphenyl sulfone only undefined

TABLE XI
MICHAEL CONDENSATIONS WITH UNSATURATED NITRILES OTHER THAN ACRYLONITRILE

Reactants	Catalyst	Product (Yield, %)	References
<i>Crotononitrile (or Allyl Cyanide) and</i>		$A = CH_3CHCH_2CN$	
Ethyl cyanoacetate	$NaOC_2H_5$	$A CH(CN)CO_2C_2H_5$ (90)	77
Ethyl α -cyanopropionate	$NaOC_2H_5$	$CH_3C(A)(CN)CO_2C_2H_5$	77
Benzyl cyanide	$NaOC_2H_5$; $NaOCH_3$	$C_6H_5CH(A)CN$ (76)	27
1-Nitropropane	Aq. $NaOH$	$C_2H_5CH(A)NO_2$ (80)	117
2-Nitropropane	$[CH_3N(C_2H_5)_3]OH$	$(CH_3)_2C(A)NO_2$ (80)	117
Fluorene	$[C_6H_5CH_2N(CH_3)_3]OH$	 (51)	282
Methyl fluorene-9-carboxylate	KOH	 (73)	291
Ethyl fluorene-9-carboxylate	KOH	 (70)	291
<i>Methacrylonitrile and</i> 1,2,3,4-Tetrahydrofluoranthene	$[C_6H_5CH_2N(CH_3)_3]OH$	1-(β -Cyanopropyl)-1,2,3,4-tetrahydrofluoranthene	754, 755

<i>γ</i> -Methoxycarbonitrile and		$A = \text{CH}_3\text{OCH}_2\text{CHCH}_2\text{CN}$	
Diethyl malonate	NaOC_2H_5	$\text{ACH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (74)	818, cf. 819
Diethyl ethylmalonate	NaOC_2H_5	$\text{AC}(\text{C}_2\text{H}_5)(\text{CO}_2\text{C}_2\text{H}_5)_2$ (38)	820
Diethyl β-methoxyethylmalonate	NaOC_2H_5	$\text{AC}(\text{CH}_2\text{CH}_2\text{OCH}_2)(\text{CO}_2\text{C}_2\text{H}_5)_2$ (40-50)	820
Diethyl β-ethoxyethylmalonate	NaOC_2H_5	$\text{AC}(\text{CH}_2\text{CH}_2\text{OC}_2\text{H}_5)(\text{CO}_2\text{C}_2\text{H}_5)_2$ (42)	820
3-Cyano-1,2,5,6-tetrahydropyridine and			
Diethyl malonate	NaOC_2H_5		87
Cyclopentylidenecarbonitrile and		(Cischoleponic acid, 2 isomers)	
Cyanoacetamide	NaOC_2H_5		821
1-Cyano-2-methyl-1-cyclohexene and			
Diethyl malonate	NaOC_2H_5	Diethyl (2-cyano-1-methylcyclohexyl)malonate (low)	822
Cyclohexylidenecarbonitrile and			
Cyanoacetamide	NaOC_2H_5		821

Note: References 491-1045 are on pp. 545-555.

* This product was obtained after hydrolysis and partial decarboxylation.

TABLE XI—Continued
MICHAEL CONDENSATIONS WITH UNSATURATED NITRILES OTHER THAN ACRYLONITRILE


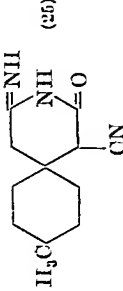
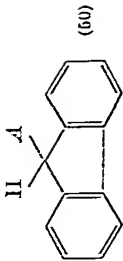
Reactants	Catalyst	Product (Yield, %)	References
(3-Methylcyclohexylidene)acetonitrile and Glymonacetamide	NaOC_2H_5	 (25)	402a
(4-Methylcyclohexylidene)acetonitrile and Glymonacetamide	NaOC_2H_5	 (26)	402a
Cinnamionitrile and Diethyl malonate Ethyl phenylacetate Benzyl cyanide <i>p</i> -Methoxybenzyl cyanide <i>m</i> -Aminobenzyl cyanide	NaOC_2H_5 NaOC_2H_5 ; NaOCH_3 NaOC_2H_5 ; NaOCH_3 NaOC_2H_5 ; NaOCH_3 NaOC_2H_5 ; NaOCH_3	$A = \text{C}_6\text{H}_5\text{CHCH}_2\text{CN}$ $A\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (83) $\text{C}_6\text{H}_5\text{CH}(A)\text{CO}_2\text{C}_2\text{H}_5$ (50) $\text{C}_6\text{H}_5\text{CH}(A)\text{CN}$ (80–87) <i>p</i> - $\text{CH}_3\text{OC}_6\text{H}_4\text{CH}(A)\text{CN}$ (23) <i>m</i> - $\text{NH}_2\text{C}_6\text{H}_4\text{CH}(A)\text{CN}$ (Two isomers: 17, 30)	290 27 27, 805 27 27
Fluorene	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	 (60)	289

TABLE XI—Continued
MICHAEL CONDENSATIONS WITH UNSATURATED NITRILES OTHER THAN ACRYLONITRILE




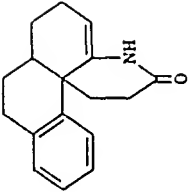
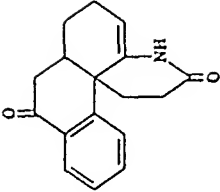
Reactants	Catalyst	Product (Yield, %)	References
1-Cyano-1,3-butadiene (Cont.) and		$A = -CH_2CH=CHCH_2CN$	
Ethyl cyanacetate	$[C_6H_5CH_2N(CH_3)_3]OH$	$(A)_2C(CN)CO_2C_2H_5$	91
Acetylacetone	$[C_6H_5CH_2N(CH_3)_3]OH$	$(A)_2C(COCH_3)_2$ (22)	91
Nitromethane	$[C_6H_5CH_2N(CH_3)_3]OH$	$(A)_3CNO_2$	293
Nitroethane	$[C_6H_5CH_2N(CH_3)_3]OH$	$CH_3CH(A)NO_2$ and $CH_3C(A)_2NO_2$ (total, 65)	293
1-Nitropropane	$[C_6H_5CH_2N(CH_3)_3]OH$	$C_2H_5CH(A)NO_2$	293
2-Nitropropane	$[C_6H_5CH_2N(CH_3)_3]OH$	$(CH_3)_2C(A)NO_2$ (77)	293
Nitrocyclohexane	$[C_6H_5CH_2N(CH_3)_3]OH$		293

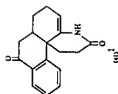
TABLE XIa
MICHAEL CONDENSATIONS WITH ACRYLAMIDE¹⁰ AND METHACRYLAMIDE¹¹

Reactants	Catalyst	Product (Yield, %)
<i>Acrylamide and</i> Cyclohexanone Acetophenone Dibenzyl ketone	NaH KOC ₄ H ₉ , <i>t</i> KOC ₄ H ₉ , <i>t</i>	2-Oxo-1,2,3,4,5,6,7,8-octahydroquinoline (10) γ -Benzoylbutyric acid* (20) [C ₆ H ₅ CH(CH ₂ CH ₂ CONH ₂) ₂] ₂ CO (48)
2-Phenylcyclohexanone	KOC ₄ H ₉ , <i>t</i>	
2-Phenylcycloheptanone	NaNH ₂	
	KOC ₄ H ₉ , <i>t</i> NaNH ₂	Lactam of β -(2-keto-1-phenylcycloheptyl)propionic acid (31) Lactam of β -(2-keto-1-phenylcycloheptyl)propionic acid (22)

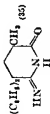
* This product was obtained after hydrolysis.

TABLE XI A—Continued
MICHAEL CONDENSATIONS WITH ACRYLAMIDE²⁹⁵ AND METHACRYLAMIDE⁸²³

Reactants <i>Acrylamide (Cont.) and</i>	Catalyst	Product (Yield, %)
4-Oxo-1,2,3,4,9,10,11,12-octahydrophenanthrene	KOC_2H_5 , t	 (50) [†]
4,9-Dioxo-1,2,3,4,9,10,11,12-octahydrophenanthrene	KOC_2H_5 , t	 (23)



NaH

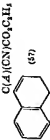
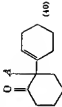
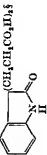
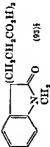
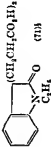
NaOC₂H₅*Methacrylamide and**Diphenylacetoneitrile*

† The yield of lactam was 23%; when the residual reaction mixture was hydrolyzed, the yield of the corresponding acid was 27%.

‡ The yield of lactam was 57%; further work up of the mother liquor yielded an additional 10% of the lactam.

TABLE XII

MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC ACID DERIVATIVES			References
Reactants	Catalyst	Product (Yield, %)	
<i>Methyl Acrylate and</i>		$A = -CH_2CH_2CO_2CH_3$	
Diethyl malonate	Na	$AH(CO_2C_2H_5)_2$ (76)	525
Diethyl acetamidomalonate	$NaOC_2H_5$	Glutamic acid* (64)	463
Ethyl acetacetate	$NaOC_2H_5$; Na	$CH_3COCH(A)CO_2C_2H_5$ (73, 38)	824, 525
Ethyl 5-ethoxy-3-oxopentanoate	Na	Methyl 5-oxo-6-heptenoate (19)†	538
Ethyl benzoylacetate	$[C_6H_5CH_2N(CH_3)_3]OH$	$C_6H_5COCH(A)CO_2C_2H_5$ (52)	536
Ethyl cyanoacetate	$NaOC_2H_5$	$NCCH(A)CO_2C_2H_5$ (73)	825
Malononitrile	$[C_6H_5CH_2N(CH_3)_3]OH$	$(A)_2C(CN)_2$	826
Diethyl 1,2-dicyano-2-methylpentane-1,5-dicarboxylate	KOC_2H_5	$(A)C(CN)(CO_2C_2H_5)C(CN)(CH_3)CH_2CH_2CO_2C_2H_5$ (65)	793
Benzyl cyanide	$NaOCH_3$; $NaNH_2$	$C_6H_5CH(A)CN$ (20-24)	27
α -Phenylpropionitrile	$NaOCH_3$	$C_6H_5C(A)(CH_3)CN$ (43)	758
α -Phenylbutyronitrile	$[C_6H_5CH_2N(CH_3)_3]OH$	$C_6H_5C(A)(C_2H_5)CN$	808
α -Isopropylbenzyl cyanide	$[C_6H_5CH_2N(CH_3)_3]OH$	$C_6H_5C(A)(C_3H_7-i)CN$	808
α -Isobutylbenzyl cyanide	$[C_6H_5CH_2N(CH_3)_3]OH$	$C_6H_5C(A)(C_4H_9-i)CN$	808
α -(2-Thienyl)benzyl cyanide	$[C_6H_5CH_2N(CH_3)_3]OH$	$C_6H_5C(A)(C_6H_5S)CN$	808
α -n-Pentylbenzyl cyanide	$[C_6H_5CH_2N(CH_3)_3]OH$	$C_6H_5C(A)(C_5H_{11-n})CN$	808
α -(3-Methylbutyl)benzyl cyanide	$[C_6H_5CH_2N(CH_3)_3]OH$	$C_6H_5C(A)(CN)CH_2CH_2CH(CH_3)_2$	808
α -(2-Pyridyl)benzyl cyanide	$[C_6H_5CH_2N(CH_3)_3]OH$	$C_6H_5C(A)(C_5H_4N)CN$	808
α -(2-Pyridyl)-p-chlorobenzyl cyanide	$[C_6H_5CH_2N(CH_3)_3]OH$	$p-ClC_6H_4C(A)(C_5H_4N)CN$	808
α -(1-Cyclohexenyl)benzyl cyanide	$[C_6H_5CH_2N(CH_3)_3]OH$	$C_6H_5C(A)(C_6H_9)CN$	808
α -Cyclohexylbenzyl cyanide	$[C_6H_5CH_2N(CH_3)_3]OH$	$C_6H_5C(A)(C_6H_{11})CN$	808
Diphenylacetoneitrile	$NaOCH_3$	$(C_6H_5)_2C(A)CN$	823
α -(p-Chlorophenyl)benzyl cyanide	$[C_6H_5CH_2N(CH_3)_3]OH$	$C_6H_5C(A)(C_6H_4Cl-p)CN$	808

Ethyl (α -tetralylidene)cyanoacetate†	NaOC_2H_5		827
2-(1'-Cyclohexenyl)cyclohexanone	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OCH}_3$		828
Oxindole	NaOC_2H_5		829
1-Methyloxindole	NaOC_2H_5		372
1-Ethylloxindole	NaOC_2H_5		829

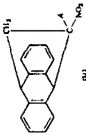
Note: References 491-1045 are on pp. 545-555.

* This acid was isolated after hydrolysis and partial decarboxylation.

† This compound was isolated by partial hydrolysis and decarboxylation, which were accompanied by elimination of one molecule of ethanol.

‡ This compound reacts in the tautomeric β,γ -unsaturated form.

§ This compound was isolated after saponification.

Methyl γ -isopropyl- γ -nitro- butyrate	$(C_3H_7)_2NH$	$(CH_3)_2CHC(A)_2NO_2$ (41)	453
	$(C_3H_7CH_2N(C_2H_5)_2)OH$	$(CH_3)_2CHC(A)_2NO_2$ (29)	
Endo(nitroethylene)anthracene	$NaOCH_3$	 (a)	813
Triethyl phosphonoacetate	$NaOC_2H_5$ Na (small amount) K (molar amount) $NaOC_2H_5$ K (molar amount) $NaOC_2H_5$ Anion exchange resin	$(C_2H_5O)_3P(O)KCH(A)CO_2C_2H_5$ (40) $(C_2H_5O)_3P(O)KCH(A)CO_2C_2H_5$ (53) $(C_2H_5O)_3P(O)K(A)_2CO_2C_2H_5$ (67) $(C_2H_5O)_3P(O)K(A)_2(C_2H_5-n)CO_2C_2H_5$ (61) $(C_2H_5O)_3P(O)K(A)_2(C_2H_5-n)CO_2C_2H_5$ (73) $ACH(CO_2C_2H_5)_2$ $ACH(CO_2C_2H_5)_2$: $(A)_2C(CO_2C_2H_5)_2$ $ACH(C_2H_5)(CO_2C_2H_5)_2$ (74) $AC(C_2H_5)(CO_2C_2H_5)_2$ (79) $AC(C_2H_5-n)(CO_2C_2H_5)_2$ (88) $AC(C_2H_5-n)(CO_2C_2H_5)_2$ (83) $AC(C_2H_5-n)(CO_2C_2H_5)_2$ (81) $AC(C_2H_5-n)(CO_2C_2H_5)_2$ (79)	121 817 817 121 817 60 490 60 835 835 835 835 835
Triethyl α -phosphonohexanoate			
Diethyl malonate			
Diethyl methylmalonate			
Diethyl ethylmalonate**			
Diethyl <i>n</i> -butylmalonate††			
Diethyl <i>n</i> -hexylmalonate**			
Diethyl <i>n</i> -octylmalonate**			
Diethyl <i>n</i> -decylmalonate**			




Note: References 491-1045 are on pp. 515-555.

§ This compound was isolated after saponification.

|| The dinitro compound was used as its potassium salt in aqueous solution; no other catalyst was employed. The dinitro compound was converted to the mononitro compound.

the dinitro compound was employed as its ar-sodium salt in aqueous solution.

†† When methyl acrylate and sodium ethoxide were employed, an 85% yield of $n\text{-C}_{11}\text{H}_{23}(\text{CO}_2\text{C}_2\text{H}_5)_2$ was obtained.

Oxindole	NaOC_2H_5		845
1-Methyloxindole	NaOC_2H_5		846
1,3-Dimethyloxindole	NaOC_2H_5		848
Nitromethane	$(\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_2)_3\text{OH})$	$(\text{A})_2\text{CHNO}_2$	452
Nitroethane	$(\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_2)_3\text{OH})$	$\text{ACH}(\text{CH}_2)_3\text{NO}_2$ (90) or $(\text{A})_2\text{C}(\text{CH}_2)_3\text{NO}_2$	830, 452
1-Nitropropane	$(\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_2)_3\text{OH})$	$\text{C}_2\text{H}_5\text{CH}(\text{A})\text{NO}_2$	830
2-Nitropropane	$(\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_2)_3\text{OH})$	$\text{C}_2\text{H}_5\text{C}(\text{A})_2\text{NO}_2$	830
β , β -Dinitroethanol	— 	$(\text{CH}_2)_3\text{C}(\text{A})\text{NO}_2$	837
Ethyl nitroacetate	$(\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_2)_3\text{OH})$	$(\text{NO}_2)_2\text{C}(\text{A})\text{CH}_2\text{OH}$ (35)	455
		$\text{ACH}(\text{NO}_2)_2\text{CO}_2\text{C}_2\text{H}_5$ (55)	455
		$\text{ACH}(\text{NO}_2)_2\text{CO}_2\text{C}_2\text{H}_5$ (22)	811
		$\text{ACH}(\text{NO}_2)_2\text{CO}_2\text{C}_2\text{H}_5$ (11)	847
	$(\text{C}_2\text{H}_5\text{N}(\text{CH}_2)_3\text{OH})$	$\text{ACH}(\text{NO}_2)_2\text{CO}_2\text{C}_2\text{H}_5$	

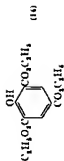
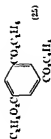
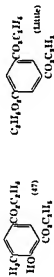
Note: References 491-1045 are on pp. 545-555.

|| The dinitro compound was used as its potassium salt in aqueous solution; no other catalyst was employed.

** In this experiment methyl acrylate was used as starting material; it was *trans*-esterified by the catalyst solution.

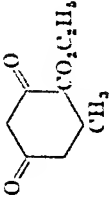
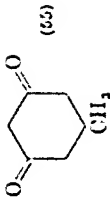
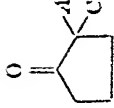
†† In this experiment, the condensation product was not isolated, but was treated directly with ethyl α -bromoisobutyrate.



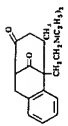

§§ This product is formed by hydrolytic fission of the cyclohexane ring.

*Ethyl β-Ethoxyacrylate and*Diethyl malonate NaOC_2H_5 307{ $\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_2)_3\text{OC}_2\text{H}_5$, $\text{C}_2\text{H}_5\text{O}_2\text{C}-\text{C}_6\text{H}_4-\text{CO}_2\text{C}_2\text{H}_5$ } 307Diethyl methylmalonate $[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_2)_3\text{OC}_2\text{H}_5$, Diethyl 3-ethoxybutane-2,4-dicarboxylate (19) and diethyl carbonate, diethyl 1-butene-1,3-dicarboxylate (18) 307 NaOC_2H_5 307*Crotonic Acid and*Kojic acid NaHCO_3 849*Note:* References 491-1045 are on pp. 545-555.

|| The dinitro compound was used as its potassium salt in aqueous solution; no other catalyst was employed.

TABLE XII—Continued
MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC ACID DERIVATIVES

Reactants	Catalyst	Product (Yield, %)	References
<i>Ethyl Crotonate and</i> Diethyl malonate	NaOC_2H_5	$A = -\text{CH}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $A\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (38, 53, 95, 98)	5, 851, 50, 850, 7, 8 50, cf. 607
Diethyl methylmalonate	NaOC_2H_5 (1/6 mole)	2-Methylbutane-1,3,3-tricarboxylic acid§ and 2-methylbutane-1,1,3-tricarboxylic acid§ (0 : 1, 90)	50, cf. 607
Ethyl phenylacetate	NaOC_2H_5 (1 mole)	2-Methylbutane-1,1,3-tricarboxylic acid§ (90) $\text{C}_6\text{H}_5\text{CH}(A)\text{CO}_2\text{C}_2\text{H}_5$ (22)	852
Ethyl 3,4-dimethoxyphenyl- acetate	NaOC_2H_5	3,4-(CH_3O) $_2\text{C}_6\text{H}_3\text{CH}(A)\text{CO}_2\text{C}_2\text{H}_5$ (76)	853
Ethyl acetoacetate	NaOC_2H_5	$\text{CH}_3\text{COCH}(A)\text{CO}_2\text{C}_2\text{H}_5$ (90)	782
		 (80, 65)	180, 851
		 (65)	855
2-Carboethoxycyclopentanone	KOC_2H_5	 triethyl 2-methylhexane-1,3,6-tricarboxylate§§	850, 857, 858

2-Carboxy-5-methylcyclopentanone	KOC_2H_5		(66)	304, 305
Ethyl cyanoacetate	NaOC_2H_5			859, 860
Ethyl α -cyanopropionate	NaOC_2H_5			77, 80
Ethyl α -cyanobutyrate	NaOC_2H_5			77
Ethyl α -cyanohydrocinnamate	NaOC_2H_5			80
Cyanoacetamide	Na enolate			349
Benzyl cyanide	NaOC_2H_5			27
1-(β -Diethylaminoethyl)-2-tetralone	NaOC_2H_5			801
Nitromethane	$[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OC}_2\text{H}_5$ $(\text{C}_2\text{H}_5)_3\text{NH}$ $(i\text{-C}_4\text{H}_9)_3\text{NH}$ K			450 450 450 817
Triethyl phosphonoacetate				
Ethyl α -chlorocrotonate and				
Ethyl acetoacetate	Na enolate			802

Note: References 491-1045 are on pp. 545-555.

§ This compound was isolated after saponification.

§§ This product is formed by hydrolytic fission of the alicyclic ring.

¶¶ This product has not been isolated, but was condensed with ethyl β -chloropropionate (ref. 859) or ethyl bromoacetate (ref. 860).

TABLE XII—Continued
MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC ACID DERIVATIVES

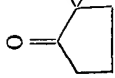
Reactants	Catalyst	Product (Yield, %)	References
<i>Ethyl β-Hydroxycrotonate and</i> Cyanacetamide	Piperidine	3-Cyano-6-hydroxy-4-methyl-2-pyridone	378
<i>Ethyl β-Aminocrotonate and</i> Malonoamide Cyanacetamide	Piperidine Piperidine	6-Hydroxy-4-methyl-2-pyridone-3-carboxamide 3-Cyano-6-hydroxy-4-methyl-2-pyridone	378 391
<i>Ethyl β-Ethoxycrotonate and</i> Cyanacetamide	Piperidine	3-Cyano-6-hydroxy-4-methyl-2-pyridone	378
<i>Ethyl γ-Acetoxycrotonate and</i> Nitromethane	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OC}_2\text{H}_5$	$\text{CH}_3\text{CO}_2\text{CH}_2\text{CH}(\text{CH}_2\text{NO}_2)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ (65)	457
<i>Ethyl γ,γ,γ-Trifluorocrotonate and</i> Nitromethane	$(\text{C}_2\text{H}_5)_3\text{N}$	$\text{CF}_3\text{CH}(\text{CH}_2\text{NO}_2)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ (68)	863
<i>Methyl Methacrylate and</i> Diethyl methylmalonate Ethyl acetoacetate	NaOC_2H_5 NaOC_2H_5	$\text{A} = -\text{CH}_2\text{CH}(\text{CH}_3)\text{CO}_2\text{CH}_3$ Triethyl pentane-2,2,4-tricarboxylate (66) $\text{CH}_3\text{COCH}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}_2\text{CH}(\text{CH}_3)\text{CO}_2\text{CH}_3$	864 782
2-Carbethoxycyclopentanone Diphenylacetoneitrile	NaOCH_3 NaOC_2H_5	 (70) $(\text{C}_6\text{H}_5)_2\text{C}(\text{A})\text{CN}$ (80)	865 823

TABLE XII—Continued
MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC ACID DERIVATIVES

Reactants	Catalyst	Product (Yield, %)	References
<i>Diethyl Malathenemalonate</i> ††† and			
Diethyl malonate	KOH, C_2H_5OH	$(C_2H_5O_2C)_2CHCH_2CH(CO_2C_2H_5)_2$ (quant.)	870
Tetraethyl propane-1,1,3,3-tetracarboxylate	KOH, C_2H_5OH	Hexaethyl pentane-1,1,3,3,5,5-hexacarboxylate	870
Ethyl o-nitrophenylacetate	$NaOC_2H_5$	$o-O_2NC_6H_4CH(CO_2C_2H_5)CH_2CH(CO_2C_2H_5)_2$ (80)	871, 829, 872
Ethyl acetoacetate	$NaOC_2H_5$	Triethyl 2-oxopentane-3,5,5-tricarboxylate (38)	867
<i>Dimethyl Maleate and</i>			
Diethyl n-butylmalonate	Not indicated	$n-C_4H_9CH(CO_2H)CH(CO_2H)CH_2CO_2H^*$	873
Diethyl isoamylmalonate	Not indicated	$i-C_5H_{11}CH(CO_2H)CH(CO_2H)CH_2CO_2H^*$	873
Diethyl n-hexylmalonate	Not indicated	$n-C_6H_{13}CH(CO_2H)CH(CO_2H)CH_2CO_2H^*$	873
Diethyl cyclohexylmalonate	Not indicated	$C_6H_{11}CH(CO_2H)CH(CO_2H)CH_2CO_2H^*$	873
Diethyl isoöctylmalonate	Not indicated	$i-C_8H_{17}CH(CO_2H)CH(CO_2H)CH_2CO_2H^*$	873
Benzyl cyanide	$NaOCH_3$	$C_6H_5CH(CN)CH(CO_2CH_3)CH_2CO_2CH_3$ (50)	27
<i>Dimethyl Maleate and</i>			
2-Nitropropane†††	$(C_2H_5)_2NH \cdot CH_3CO_2H$ C_2H_5NH	$(CH_3)_2C(NO_2)CH(CO_2CH_3)CH_2CO_2CH_3$ (69) $(CH_3)_2C(NO_2)CH(CO_2CH_3)CH_2CO_2CH_3$ (80); $(CH_3)_2C=C(CO_2CH_3)CH_2CO_2CH_3$ (16)	882 882
Triethyl phosphonacetate	$(C_2H_5)_2NH$ $NaOC_2H_5$	$(CH_3)_2C(NO_2)CH(CO_2CH_3)CH_2CO_2CH_3$ (85) $(C_2H_5O)_2P^-(O)CH(CO_2C_2H_5)CH(CO_2CH_3)CH_2CO_2CH_3$ (13)	832 124
<i>Diethyl Maleate and</i>			
Diethyl malonate	Na; KOH, acetal	$A = -CH(CO_2C_2H_5)CH_2CO_2C_2H_5$ $A = CH(CO_2C_2H_5)_2$ (72)	483, 6, 517, 518


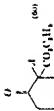
Ethyl phenylacetate ethyl acetoacetate	$\text{Na}(\text{OC}_2\text{H}_5)_2$ KOH , acetal	$\text{C}_6\text{H}_5\text{CH}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}_3\text{COCH}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (72)	874 48
	Na ; $\text{Na}(\text{OC}_2\text{H}_5)_2$		310, 875
2-Carboethoxycyclohexanone	Piperidine		870
Isopropyl cyanide	$\text{K}(\text{OC}_2\text{H}_5)_2$ $\text{Na}(\text{OC}_2\text{H}_5)_2$ KOH , acetal	Tetraethyl hexane-1,2,3,4-tetracarboxylate (90)§§ $\text{C}_2\text{H}_5\text{CH}(\text{A})\text{CN}$ (52-58) $\text{C}_2\text{H}_5\text{CH}(\text{A})\text{CN}$ (74)	870 27 483, 517,
2-Methylcyclohexane 1,2-dione	$\text{Na}(\text{OC}_2\text{H}_5)_2$	Triethyl 3-methyl-4-oxoheptane-1,2,7-tricarboxylate (62)§§	518 844
Isomethyl fumarate and isomethyl malonate ethyl cyanoacetate	$(\text{C}_2\text{H}_5)_3\text{NH}$ $(\text{C}_2\text{H}_5)_3\text{NH}$ $(\text{C}_2\text{H}_5)_3\text{NH}$	$\text{A} = -\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{ACH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (5) $\text{ACH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (10) $(\text{CH}_3)_3\text{C}(\text{A})\text{NO}_2$ (80-85)	18 18 872
2-Nitro-3-oxofuran			

TABLE XII—Continued
MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC ACID DERIVATIVES

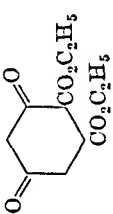
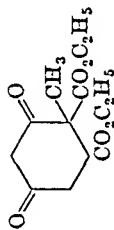
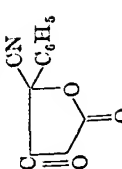
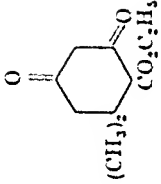
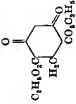
Reactants	Catalyst	Product (Yield, %)	References
<i>Diethyl fumarate (Cont.) and</i> Diethyl malonate	Na; NaOC ₂ H ₅	$A = -CH(CO_2C_2H_5)CH_2CO_2C_2H_5$ $ACH(CO_2C_2H_5)_2$ (90, 55)	77, 5, 7, 8, 6, 877, 878
Diethyl methylmalonate	NaOC ₂ H ₅	$AC(CH_3)(CO_2C_2H_5)_2$	77, 878, 7, 8
Diethyl ethylmalonate	NaOC ₂ H ₅	$AC(C_2H_5)(CO_2C_2H_5)_2$ (61, 80)	5, 879, 7, 8, 77, 878
Diethyl isopropylmalonate	NaOC ₂ H ₅	$AC(C_3H_7)(CO_2C_2H_5)_2$	7, 878
Diethyl benzylmalonate	NaOC ₂ H ₅	$AC(CH_2C_6H_5)(CO_2C_2H_5)_2$ (23-31)§§§	50, 880
Ethyl acetoacetate	Na; NaOC ₂ H ₅	$CH_3COCH(A)CO_2C_2H_5$ and 	875
Ethyl methylacetoacetate	NaOC ₂ H ₅	$CH_3COC(CH_3)(A)CO_2C_2H_5$ and 	316, 878
Ethyl ethylacetoacetate	NaOC ₂ H ₅	$CH_3COC(C_2H_5)(A)CO_2C_2H_5$	875
Ethyl propionylacetate	NaOC ₂ H ₅	$C_2H_5COCH(A)CO_2C_2H_5$	879
Ethyl benzylacetoacetate	NaOC ₂ H ₅	$CH_3COC(CH_2C_6H_5)(A)CO_2C_2H_5$	875
Ethyl cyanoacetate	Na	$NCCH(A)CO_2H$; $NCCH(A)CO_2C_2H_5$	316
Benzyl cyanide	NaOC ₂ H ₅		881

TABLE XII—Continued
MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC ACID DERIVATIVES

Reactants	Catalyst	Product (Yield, %)	References
<i>Ethyl β,β-Dimethylacrylate and</i> Diethyl malonate	KOC_2H_5 ; NaOC_2H_5	$\text{A} = (\text{CH}_3)_2\text{CCH}_2\text{CO}_2\text{C}_2\text{H}_5$ (35)	880, 11, 24
Ethyl acetoacetate	Na		415
Ethyl α -cyanopropionate Benzyl cyanide	Na NaOC_2H_5	$\text{CH}_3\text{C(A)(CN)CO}_2\text{C}_2\text{H}_5 \cdots$ $\text{C}_6\text{H}_5\text{CH(A)CN}$ (43)	23 27
<i>Ethyl Tiglate and</i> Diethyl malonate	NaOC_2H_5	$\text{A} = -\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$ $\text{A} = -\text{CH}(\text{CH}_3)_2$ (15, 63)	50, 50, cf. 887
Diethyl ethylmalonate Ethyl phenylacetate Ethyl cyanoacetate	NaOC_2H_5 K Na enolate	$\text{A} = -\text{C}(\text{C}_2\text{H}_5)(\text{CO}_2\text{C}_2\text{H}_5)_2$ (14) $\text{C}_6\text{H}_5\text{CH(A)CO}_2\text{C}_2\text{H}_5$ $\text{A} = -\text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (42, 65)	59 852 50, 887, 888
<i>Ethyl α-Ethylacrylate and</i> Ethyl acetoacetate	NaOC_2H_5	$\text{CH}_3\text{COCH}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}_2\text{CH}(\text{C}_2\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5$ diethyl α -ethylglutarate	880

<i>Dimethyl Glutaconate and</i>		$A = \text{---CH}(\text{CH}_2\text{CO}_2\text{CH}_3)_2$	
Methyl cyanoacetate	NaOCH_3	$\text{ACH}(\text{CN})\text{CO}_2\text{CH}_3$ (46)	890
Ethyl cyanoacetate	$\text{Na}; \text{NaOCH}_3; \text{NaOC}_2\text{H}_5$	$\text{ACH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (84)	890, 892
Nitromethane	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	ACH,NO_2 (51)	891
<i>Dimethyl Ethyldienemalonate and</i>			
Deoxybenzoin	NaOCH_3	$\text{C}_6\text{H}_5\text{COCH}(\text{C}_6\text{H}_5)\text{CH}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{H}$ (55)*	163
<i>Diethyl Ethyldienemalonate and</i>		$A = \text{CH}_2\text{CHCH}(\text{CO}_2\text{C}_2\text{H}_5)_2$	
Diethyl malonate††††	None; Na	$\text{ACH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (95)	892, 893
Ethyl acetoacetate	NaOC_2H_5		14
Nitromethane	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	ACH,NO_2 (89)	457
<i>Ethyl Ethyldienemalonate†††† and</i>			
Ethyl malonamate	$\text{KOH}; (\text{C}_2\text{H}_5)_3\text{NH}$	$\text{CH}_3\text{CH}[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)\text{CONH}_2]_2$ (73)	895

Note: References 491-1045 are on pp. 545-555.

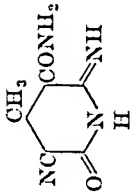

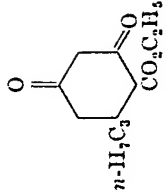
* This acid was isolated after hydrolysis and partial decarboxylation.


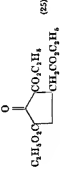
.... The product has not been isolated, but has been methylated directly.

††† The same reaction takes place when acetaldehyde and diethyl malonate react in the presence of secondary amines; the yield is from 11 (ref. 887) to 55% (ref. 894).

†††† This material is formed *in situ* from the aldehyde or ketone and the derivative of malonic or cyanoacetic acid.

TABLE XII—Continued
MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC ACID DERIVATIVES

Reactants	Catalyst	Product (Yield, %)	References
<i>Ethylidenecyanoacetamide†††† and</i>			
Cyanoacetamide	KOH	$\text{CH}_3\text{CH}[\text{CH}(\text{CONH}_2)\text{CN}]_2,$ 	896
<i>Ethylidenemalononitrile†††† and</i>			
Malononitrile	Piperidine	$\text{CH}_3\text{CH}[\text{CH}(\text{CN})_2]_2$	897
<i>Ethyl α-Ethylcrotonate and</i>			
Diethyl malonate	NaOC_2H_5	$A = \text{CH}_3\text{CHCH}(\text{C}_2\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5$ 	59
Diethyl ethylmalonate	NaOC_2H_5		59
Ethyl cyanoacetate	NaOC_2H_5		77
<i>Ethyl β-n-Propylacrylate and</i>			
Ethyl acetate	NaOC_2H_5		898
Nitromethane	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OC}_4\text{H}_9$	$n\text{-C}_3\text{H}_7\text{CH}(\text{CH}_2\text{NO}_2)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ (71)	116
<i>Ethyl β-Isopropylacrylate and</i> Diethyl malonate	NaOC_2H_5	$i\text{-C}_3\text{H}_7\text{CH}(\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5)\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$	880

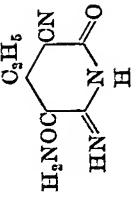
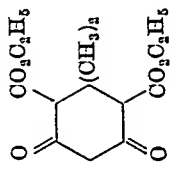
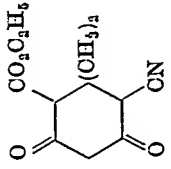
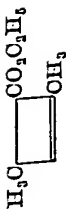
<i>Ethyl α-n-Butylacrylate and</i> <i>Ethyl cyanoacetate</i>	NaOC ₄ H ₉	CNCH(CO ₂ C ₂ H ₅)CH ₂ CH(C ₄ H ₉ -n)CO ₂ C ₂ H ₅ (54)	889
<i>Methyl β-n-Pentylacrylate and</i>			
<i>Ethyl acetooacetate</i>	NaOC ₄ H ₉	 <p style="text-align: center;">(71)</p>	180
<i>Dimethyl 1,2-Dihydromuconate and</i>			
<i>Ethyl cyanoacetate</i>	NaOC ₂ H ₅	(β-Carboxymethyl)adipic acid (79)*	899
<i>Ethyl phenethylcyanoacetate</i>	KOC ₂ H ₅	C ₆ H ₅ CH ₂ CH ₂ C(CN)(CO ₂ C ₂ H ₅)CH(CH ₂ CO ₂ C ₂ H ₅)CH ₂ CH ₂ CO ₂ C ₂ H ₅ (46)	899
<i>Diethyl 1,2-Dihydromuconate and</i>			
<i>Diethyl malonate</i>	NaOC ₂ H ₅	C ₂ H ₅ O ₂ CCH ₂ CH ₂ CH(CH ₂ CO ₂ C ₂ H ₅)CH(CO ₂ C ₂ H ₅) ₂ (50),	900
<i>Ethyl 4,4,5,5,6,6-Heptafluoro-2-hexenoate and</i> <i>Nitromethane</i>	(C ₂ H ₅) ₂ N	 <p style="text-align: center;">(25)</p>	903
<i>Diethyl Propylidenemalonate and</i> <i>Diethyl malonate</i>	Enolate	C ₂ H ₅ CH[CH(CO ₂ C ₂ H ₅) ₂] ₂ (quant)	901



Note: References 491-1015 are on pp. 545-555.

* This acid was isolated after hydrolysis and partial decarboxylation

**** This material is formed *in situ* from the aldehyde or ketone and the derivative of malonic or cyanoacetic acid.

TABLE XII—Continued
MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC ACID DERIVATIVES

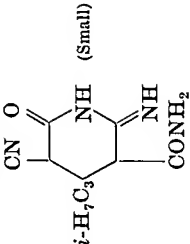
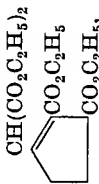
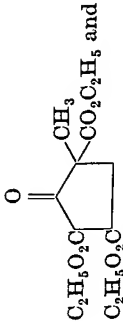
Reactants	Catalyst	Product (Yield, %)	References
<i>Propylidenecyanoacetamide</i> †††† and Cyanoacetamide	KOH	$C_2H_5CH[CH(CONH_2)CN]_2$ and 	896
<i>Diethyl Isopropylidenemalonate</i> and Diethyl malonate	$NaOC_2H_5$; enolate	$(CH_3)_3C[CH(CO_2C_2H_5)_2]_2$ (95, 30, 8)	901, 902, 903, 904 905, 415
Ethyl acetoacetate	$NaOC_2H_5$	$CH_3COCH(CO_2C_2H_5)C(CH_3)_2CH(CO_2C_2H_5)_2$, 	
Cyanoacetone§§§§	$NaOC_2H_5$		415
Acetylacetonone	$NaOC_2H_5$		415

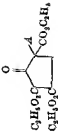
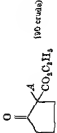
<i>Ethyl Isopropylidenecyanoacetate</i> †††† and Ethyl cyanoacetate Nitromethane	$(C_2H_5)_2NHCN$ $NaOCH_3$	$(CH_3)_2C[CH(CN)CO_2C_2H_5]_2$ (10) β,β -Dimethylglutarimide (quant.) Ethyl α -cyano- β,β -dimethyl- γ -nitrobutyrate (74)	906 821 907
<i>n</i> -Ethoxymethyl-2-hexenoate and Diethyl malonate	Na	$C_6H_5CH(CH_2OC_2H_5)CH(CH_2CO_2C_2H_5)CH(CO_2C_2H_5)_2$ (79)	908
<i>Ethyl 4,4-Diethoxymethyl-2-hexenoate</i> and Diethyl malonate	$NaOC_2H_5$	$C_6H_5CH[CH(OC_2H_5)_2]CH(CH_2CO_2C_2H_5)CH(CO_2C_2H_5)_2$ (48)	909
<i>n</i> -Butylidenecyanoacetamide††††† and Cyanooacetamide	KOH	$n-C_4H_9CH[CH(CN)CONH_2]_2$ and $n-H_7C_2$ 	896
<i>Diethyl Isobutylidenemalonate</i> ††††† and Diethyl malonate	Piperidine; $(C_2H_5)_2NH$	$(CH_3)_2CHCH[CH(CO_2C_2H_5)_2]_2$ (41)	894
<i>Ethyl Isobutylidenecyanoacetate</i> and Ethyl acetosuccinate	$NaOC_2H_5$		415

Note: References 491-1045 are on pp. 545-555.

†††† This material is formed *in situ* from the aldehyde or ketone and the derivative of malonic or cyanoacetic acid.
§§§§ Instead of cyanoacetone, α -methylisoxazole was employed.

TABLE XII—Continued

MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC ACID DERIVATIVES			References
Reactants	Catalyst	Product (Yield, %)	
<i>Isobutyldenecyanoacetamide</i> †††† and Cyanoacetamide	$(C_2H_5)_2NH$	$(CH_3)_2CHCH[CH(CN)CONH_2]_2$ (79) 	910
<i>Diethyl Itaconate and</i> Diethyl malonate	$NaOC_2H_5$	$A = -CH_2CH(CO_2C_2H_5)CH_2CO_2C_2H_5$ A = triethyl cyclopentanone-2,3,5-tri-carboxylate, ethyl cyclopentanone-3-carboxylate, diethyl cyclopentanone-2,4- (or 2,3-) dicarboxylate, 	8, 317, 911, 912
<i>Diethyl methylmalonate</i>	$NaOC_2H_5$	$C_2H_5O_2CCH_2CH(CO_2C_2H_5)CH_2CH_2CO_2C_2H_5$  $AC(CH_3)(CO_2C_2H_5)_2$ (small)	317, 406

Tetraethyl 1,1,2,3-butanetetra-carboxylate	NaOC ₂ H ₅		911
Ethyl acetoacetate	NaOC ₂ H ₅	CH ₃ COCH(A)CO ₂ C ₂ H ₅	316
2-Carboethoxycyclopentanone	[C ₂ H ₅ CH ₂ N(CH ₃) ₃]OH	 (90 crude)	913
Ethyl cyanoacetate	NaOC ₂ H ₅	ACH(CN)CO ₂ C ₂ H ₅	316
Nitromethane	(C ₂ H ₅) ₂ NH; (1-C ₂ H ₅) ₂ NH (1-C ₂ H ₅) ₃ NH	ACH ₂ NO ₂ (25)	891
Nitroethane		CH ₃ CH(A)NO ₂ (40)	891
Diethyl Mesaconate and Diethyl malonate	NaOC ₂ H ₅	C ₂ H ₅ O ₂ CCH(CH ₃)CH(CO ₂ C ₂ H ₅)CH(CO ₂ C ₂ H ₅) ₂ (60-75)	6, 317
Diethyl Citraconate and Diethyl malonate	Na enolate NaOC ₂ H ₅ NaOC ₂ H ₅	C ₂ H ₅ O ₂ CCH ₂ C(CH ₃)(CO ₂ C ₂ H ₅)CH(CO ₂ C ₂ H ₅) ₂ (72) C ₂ H ₅ O ₂ CCH ₂ CH(CO ₂ C ₂ H ₅)CH ₂ CH(CO ₂ C ₂ H ₅) ₂ (50)¶¶¶ 2,3,5-Tricarboethoxycyclopentanone	316, 317 316 316

Note: References 491-1045 are on pp 543-555

††† This material is formed *in situ* from the aldehyde or ketone and the derivative of malonic or cyanoacetic acid.

¶¶¶ Instead of diethyl itaconate, diethyl citraconate, which isomerizes under the conditions of the experiment, was employed.

¶¶¶ The citraconate is isomerized to itaconate.

TABLE XII—Continued


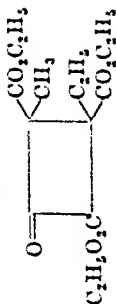
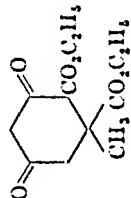
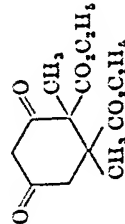
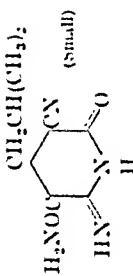
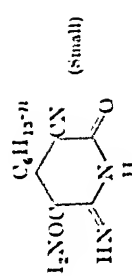
MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC ACID DERIVATIVES			
Reactants	Catalyst	Product (Yield, %)	References
Diethyl Citraconate (Cont.) and Diethyl malonate (Cont.)	NaOC_2H_5	Diethyl itaconate, diethyl mesaconate, 3-carbethoxycyclopentanone, 2,3-(or 3,4-)dicarboethoxycyclopentanone, 2,3,5-tricarboethoxycyclopentanone, $\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ 	317, 912; cf. 5, 6, 8, 911
Diethyl ethylmalonate	Na enolate		5
Ethyl acetoacetate	Na ; dry NaOC_2H_5	$\text{CH}_3\text{COCCH}(\text{CO}_2\text{C}_2\text{H}_5)\text{C}(\text{CH}_3)(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$; 	310
Ethyl methylacetoacetate	Na	$\text{CH}_3\text{COC}(\text{CH}_3)(\text{CO}_2\text{C}_2\text{H}_5)\text{C}(\text{CH}_3)(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$; 	310

TABLE XII—Continued
MICHAEL CONDENSATIONS WITH ALIPHATIC α,β -ETHYLENIC ACID DERIVATIVES

Reactants	Catalyst	Product (Yield, %)	References
<i>Diethyl Isoamylidenmalonate</i> ++++ and Diethyl malonate	Na enolate; piperidine; (C ₂ H ₅) ₂ NH	<i>i</i> -C ₄ H ₉ CH[CH(CO ₂ C ₂ H ₅) ₂] ₂ (63)	894, 878, 917, 918
<i>Isoamylidencyanoacetic Acid</i> ++++ and Cyanoacetic acid	Piperidine	α,α' -Dicyano- β -isobutylglutaric acid	917
<i>Isoamylidencyanoacetamide</i> ++++ and Cyanacetamide	(C ₂ H ₅) ₂ NH		910
<i>Ethyl (3-Pentylidene)cycanoacetate</i> ++++ and Ethyl cyanoacetate	NH ₃	β,β' -Diethylglutarimide (quant.)	821
<i>Diethyl Heptylidencmalonate</i> ++++ and Diethyl malonate	Piperidine; (C ₂ H ₅) ₂ NH	<i>n</i> -C ₄ H ₁₃ CH[CH(CO ₂ C ₂ H ₅) ₂] ₂	894
<i>Heptylidencyanoacetic Acid</i> ++++ and Cyanoacetic acid	Piperidine	<i>n</i> -C ₄ H ₁₃ CH[CH(CN)(CO ₂ H)] ₂	917
<i>Heptylidencyanoacetamide</i> ++++ and Cyanacetamide	Piperidine	<i>n</i> -C ₄ H ₁₃ CH[CH(CN)(CONH ₂) ₂] ₂ (87), 	910

<i>Triethyl Ethylenetricarboxylate and</i> Diethyl malonate	NaOC ₂ H ₅	$(C_2H_5O_2C)_2CHCH(CO_2C_2H_5)CH(CO_2C_2H_5)_2$	878, 919
<i>Triethyl 1-Propylene-1,1,2-tricarboxylate and</i> Diethyl malonate	Na enolate	$(C_2H_5O_2C)_2CHCH(CO_2C_2H_5)CH(CO_2C_2H_5)_2$ (43 49)	920
<i>Triethyl 1-Propylene-2,3,3-tricarboxylate and</i> Diethyl malonate	Na enolate	$(C_2H_5O_2C)_2CHCH(CO_2C_2H_5)CH(CO_2C_2H_5)_2$ (51)	920
<i>Tetraethyl Ethylenetricarboxylate and</i> Diethyl malonate	Na	Tricarballic acid*	893, 878
<i>Tetraethyl 1-Propylene-1,1,3,3-tetracarboxylate and</i> Ethyl cyanoacetate	Piperidine	Diethyl γ-carbalthoxy-α-cyanoglutarate and diethyl malonate	921
	NaOC ₂ H ₅	Diethyl γ-carbalthoxy-α-cyanoglutarate, diethyl malonate, and diethyl α,γ-dicyanoglutarate	916
<i>Triethyl 3-Cyano-1-propylene-1,1,3-tricarboxylate and</i> Ethyl cyanoacetate	NaOC ₂ H ₅	Diethyl α,γ-dicyanoglutarate and diethyl malonate	916
<i>Tetraethyl 1-Butene-1,1,3,3-tetracarboxylate and</i> Ethyl cyanoacetate	NaOC ₂ H ₅	Diethyl γ-carbalthoxy-α-cyanoglutarate and diethyl methylnalonate	916

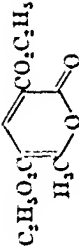
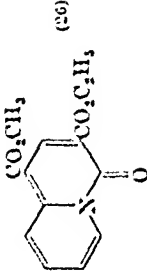
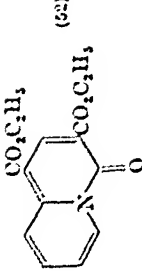
Note: References 491-1005 are on pp. 545-555.

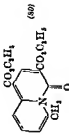



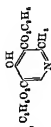
* This acid was isolated after hydrolysis and partial decarboxylation.

†††† This material is formed *in situ* from the aldehyde or ketone and the derivative of malonic or cyanoacetic acid.

TABLE XIII

MICHAEL CONDENSATIONS WITH ETHYL ETHOXYMETHYLENEMALONATE, DIETHYL ETHOXYMETHYLENEMALONATE,
AND DIETHYL AMINOMETHYLENEMALONATE

Reactants	Catalyst	Product (Yield, %)	References
<i>Ethyl Ethoxymethylenemalonate and</i> <i>Ethyl acetoacetate</i>	NaOC_2H_5		310
<i>Diethyl Ethoxymethylenemalonate and</i> <i>Diethyl malonate</i>	NaOC_2H_5	$(\text{C}_2\text{H}_5\text{O}_2\text{C})_2\text{C}=\text{CHCH}(\text{CO}_2\text{C}_2\text{H}_5)_2$	922
<i>Ethyl phenylacetate</i>	NaOC_2H_5	Diethyl 1-hydroxynaphthalene-2,4-dicarboxylate*	308
<i>Ethyl p-chlorophenylacetate</i>	NaOC_2H_5	Diethyl 7-chloro-1-hydroxynaphthalene-2,4-dicarboxylate* (7) and α -(p-chlorophenyl)glutaconic acid (11)†	309
<i>Ethyl p-bromophenylacetate</i>	NaOC_2H_5	Diethyl 7-bromo-1-hydroxynaphthalene-2,4-dicarboxylate* (11) and 7-bromo-1-hydroxynaphthalene-2,4-dicarboxylic acid (13)†	309
<i>Ethyl α-naphthylacetate</i>	NaOC_2H_5	1-Hydroxyphenanthrene-2,4-dicarboxylic acid (5)† and α -(1-naphthyl)glutaconic acid†	309
<i>Methyl 2-pyridylacetate</i>	None		923
<i>Ethyl 2-pyridylacetate</i>	None		923

Ethyl 6-methyl-2-pyridylacetate	None		924
Ethyl acetoacetate	NaOOC_2H_5		310
Ethyl β -aminocrotonate	None		441
Diethyl 2-Aminoethylene-1,1-dicarboxylate and			
Ethyl acetoacetate	HCl		441
	Na enolate		441

Note: References 491-1045 are on pp. 545-555.

* This compound could be isolated only after distillation of the crude condensation product. Direct hydrolysis of this product proved that it consisted of diethyl α -carbethoxy- γ -phenylglutaconate, $\text{C}_6\text{H}_5\text{O}_2\text{CCH}(\text{C}_6\text{H}_5)\text{CH}=\text{C}(\text{CO}_2\text{C}_2\text{H}_5)_2$.

† This acid was present in the crude product in the form of its ester, but was not isolated as such.

TABLE XIV

MICHAEL CONDENSATIONS WITH ALIPHATIC DIENIC AND TRIENIC ESTERS

Reactants	Catalyst	Product (Yield, %)	References
<i>Methyl 1,3-Butadiene-1-carboxylate and</i> Dimethyl malonate Ethyl α -cyanopropionate	NaOCH_3 ; Na NaOCH_3 (1/8 mole)	$A = \text{---CH}_2\text{CH}=\text{CHCH}_2\text{CO}_2\text{CH}_3$ $A\text{CH}(\text{CO}_2\text{CH}_3)_2$ (75) $\text{CH}_3\text{C}(A)(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$	397, 925, 926 926
<i>Methyl Sorbate and</i> Dimethyl malonate	NaOCH_3	$A = \text{CH}_3\text{CHCH}=\text{CHCH}_2\text{CO}_2\text{CH}_3$ $A\text{CH}(\text{CO}_2\text{CH}_3)_2$ and $\text{CH}_3\text{CH}=\text{CHCHCH}_2\text{CO}_2\text{CH}_3$ $\text{CH}(\text{CO}_2\text{CH}_3)_2$ (Mixture 9:1; 60-70, 80)	925-926, 927, 173
Ethyl α -cyanopropionate Nitromethane Methyl γ -nitrobutyrate	NaOCH_3 (1/8 mole) $(i\text{-C}_3\text{H}_7)_2\text{NH}$ $(i\text{-C}_3\text{H}_7)_2\text{NH}$	$A\text{C}(\text{CH}_3)(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (60-70) $A\text{CH}_2\text{NO}_2$ (21) $\text{O}_2\text{NCH}(A)\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3$ (32)	926 110 110
<i>Ethyl Sorbate and</i> Diethyl malonate Ethyl cyanoacetate	Na NaOC_2H_5	$\text{HO}_2\text{CCH}_2\text{CH}=\text{CHCH}(\text{CH}_3)\text{CO}_2\text{H}^*$ $\text{CH}_3\text{CHCH}=\text{CHCH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}(\text{CN})(\text{CO}_2\text{C}_2\text{H}_5)$ (77) and $\text{CH}_3\text{CH}=\text{CHCHCH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (9)	928 397

Ethyl acetoacetate	KOC_2H_5	$\text{CH}_3\text{CHCH}=\text{CHCH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}(\text{COCH}_3)\text{CO}_2\text{C}_2\text{H}_5$ (75)	488
<i>Ethyl α-Methylsorbate and</i> Ethyl cyanoacetate	NaOC_2H_5	$\text{CH}_3\text{CHCH}=\text{CHCH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (67)	397
<i>Ethyl β-Methylsorbate and</i> Diethyl malonate	NaOC_2H_5	$\text{CH}_3\text{CHCH}=\text{C}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ and $\text{CH}_3\text{CH}=\text{CHC}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (Mixture 9 1, 39-42)	173
Ethyl cyanoacetate	NaOC_2H_5	$\text{CH}_3\text{CHCH}=\text{C}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ and $\text{CH}_3\text{CH}=\text{CHC}(\text{CH}_3)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (66)	397

Note: References 491-1015 are on pp. 545-555.

* This product was obtained after hydrolysis and partial decarboxylation

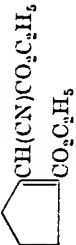
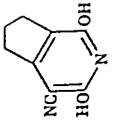
TABLE XIV—Continued
MICHAEL CONDENSATIONS WITH ALIPHATIC DIENIC AND TRIENIC ESTERS

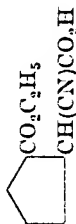
Reactants	Catalyst	Product (Yield, %)	References
<i>Ethyl γ-Methylsorbate and</i> Ethyl cyanacetate	NaOC_2H_5	$\text{CH}_3\text{CHC}(\text{CH}_3)=\text{CHCH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\quad \quad \quad $ $\quad \quad \quad \text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$	173
		and	
		$\text{CH}_3\text{CH}=\text{C}(\text{CH}_3)\text{CHCH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\quad \quad \quad $ $\quad \quad \quad \text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$	
		(Mixture 1:3; 18–40)	
<i>Methyl Hexa-1,3,5-triene-1-carboxylate and</i> Dimethyl malonate	NaOC_2H_5	Mixture of isomers of the formula $\text{C}_{13}\text{H}_{18}\text{O}_6$ (44)	929
<i>Methyl Hepta-1,3,5-triene-1-carboxylate and</i> Dimethyl malonate	NaOCH_3	$\text{CH}_3\text{CHCH}=\text{CHCH}=\text{CHCH}_2\text{CO}_2\text{CH}_3$ $\quad \quad \quad $ $\quad \quad \quad \text{CH}(\text{CO}_2\text{CH}_3)_2$	930
		and	
		$\text{CH}_3\text{CH}=\text{CHCH}=\text{CHCHCH}_2\text{CO}_2\text{CH}_3$ $\quad \quad \quad $ $\quad \quad \quad \text{CH}(\text{CO}_2\text{CH}_3)_2$	
		(Mixture 7:1; 74)	




<i>Dimethyl Penta-1,3-diene-1,1-dicarboxylate and</i> Methyl cyanosuccinate	NaOCH ₃	$\begin{array}{c} \text{CH}_2\text{CHCH}=\text{CHCH}(\text{CO}_2\text{CH}_3)_2 \\ \\ \text{CH}(\text{CN})\text{CO}_2\text{CH}_3 \end{array}$	379
		and	
		$\begin{array}{c} \text{CH}_2\text{CH}=\text{CHCHCH}(\text{CO}_2\text{CH}_3)_2 \\ \\ \text{CH}(\text{CN})\text{CO}_2\text{CH}_3 \end{array}$	
<i>Methyl α-Carbomethoxy-δ-methylsuccinate and</i> Dimethyl malonate	NaOCH ₃	$(\text{CH}_3)_2\text{C}=\text{CHCH}[\text{CH}(\text{CO}_2\text{CH}_3)_2]_2$ (83)	381
<i>Diethyl Muconate and</i> Diethyl malonate	Na NaOC ₂ H ₅ (small quant.)	$\begin{array}{l} \text{C}_2\text{H}_5\text{O}_2\text{CCH}_2\text{CH}_2\text{C}(=\text{CHCO}_2\text{C}_2\text{H}_5)\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2 \text{ (32, 90)} \\ \text{C}_2\text{H}_5\text{O}_2\text{CCH}_2\text{CH}=\text{CHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2 \end{array}$	931, 326 932
Ethyl cyanosuccinate	NaOC ₂ H ₅	$\text{C}_2\text{H}_5\text{O}_2\text{CCH}_2\text{CH}_2\text{C}(=\text{CHCO}_2\text{C}_2\text{H}_5)\text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (90)	326

Note: References 491-1045 are on pp. 545-555.

TABLE XV
MICHAEL CONDENSATIONS WITH ALICYCLIC α,β -ETHYLENIC ESTERS

Reactants	Catalyst	Product (Yield, %)	References
<i>Methyl 1-Cyclobutene-1-carboxylate and</i>			
Diethyl malonate	$\text{KOC}_4\text{H}_9\text{-}t$	Diethyl (2-carbomethoxycyclobutyl)malonate (54)	933
Ethyl cyanoacetate	$\text{KOC}_4\text{H}_9\text{-}t$	Ethyl (2-carbomethoxycyclobutyl)cyanoacetate (52)	933
<i>Methyl 3,3-Dimethyl-1-cyclobutene-1-carboxylate and</i>			
Diethyl malonate	$\text{KOC}_4\text{H}_9\text{-}t$	Diethyl (4-carbomethoxy-2,2-dimethylcyclobutyl)malonate (57)	933
Ethyl cyanoacetate	$\text{KOC}_4\text{H}_9\text{-}t$	Ethyl (4-carbomethoxy-2,2-dimethylcyclobutyl)cyanoacetate (9)	933
<i>Ethyl 1-Cyclopentene-1-carboxylate and</i>			
Diethyl malonate	NaOC_2H_5	$\text{A} \cdot \text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (80-85)	92
Ethyl acetate	NaOC_2H_5	$\text{A} \cdot \text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$ (23), $\text{CH}_3\text{COCH}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (8)	93
Ethyl cyanoacetate	NaOC_2H_5	$\text{A} \cdot \text{CH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (30-35)	92, 934, 935
<i>Ethyl 2-Hydroxy-1-cyclopentene-1-carboxylate and</i>			
Ethyl cyanoacetate	Piperidine; KOC_2H_5	 (50, 59)	936
Cyanoacetamide	Piperidine	 (58)	937

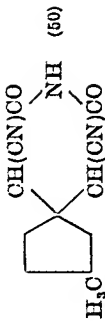
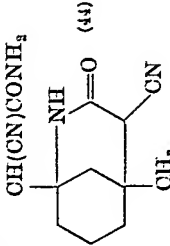
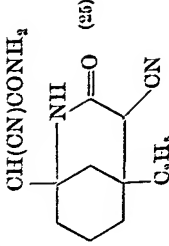


<i>Ethyl 1-Cyclohexene-1-carboxylate and</i>			
Diethyl malonate	NaOC ₂ H ₅	ACH(CO ₂ C ₂ H ₅) ₂ (40)	59, 938
Diethyl methylmalonate	NaOC ₂ H ₅	AC(CH ₃)(CO ₂ C ₂ H ₅) ₂ (6)	59
Ethyl cyanoacetate	NaOC ₂ H ₅ ; KOC ₂ H ₅ ; piperidine	ACH(CN)(CO ₂ C ₂ H ₅) (74, 35, 18)	939
	NaOC ₂ H ₅	AC(CN)(CO ₂ C ₂ H ₅)(CH ₃ CO ₂ C ₂ H ₅)*	940
<i>Ethyl 2-Hydroxycyclohexene-1-carboxylate and</i>			
Cyanoacetamide	Pyridine		398
			941
<i>Ethyl 2-Aminocyclohexene-1-carboxylate and</i>			
Cyanoacetamide	None	4-Cyano-1-hydroxy-3-oxo-2,3,5,6,7,8-hexahydroisoquinoline	398
Malonamide	Piperidine	1-Hydroxy-3-oxo-2,3,5,6,7,8-hexahydroisoquinoline-4-carboxamide	391

Note: References 491-1045 are on pp. 545-555.

* This compound was obtained by direct treatment of the condensation product with ethyl bromoacetate.

TABLE XV—Continued
MICHAEL CONDENSATIONS WITH ALICYCLIC α,β -ETHYLENIC ESTERS

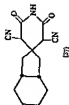
Reactants	Catalyst	Product (Yield, %)	References
<i>Ethyl 4-Methyl-1-cyclohexene-1-carboxylate and Ethyl cyanoacetate</i>	NaOC_2H_5	Ethyl 1-carbethoxy-4-methylcyclohexane-2-cyanoacetate†	942
<i>Ethyl (3-Methylcyclopentylidene)cycanoacetate† and Ethyl cyanoacetate</i>	NH_3	 (50)	943
<i>Ethyl Cyclohexylidene-cycanoacetate† and Ethyl cyanoacetate</i>	NaOC_2H_5	Cyclohexane-1,1-diacetic acid	221
<i>Ethyl (3-Methyl-2-cyclohexenylidene)cycanoacetate† and Ethyl cyanoacetate</i>	NH_3	 (44)	649
<i>Ethyl (3-Ethyl-2-cyclohexenylidene)cycanoacetate† and Ethyl cyanoacetate</i>	NH_3	 (25)	649

Ethyl (cis-2-Hydrindanylidene)cynoacetate† and

Ethyl cyanoacetate

NH₂

90

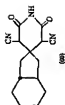


Ethyl (trans-2-Hydrindanylidene)cynoacetate‡ and

Ethyl cyanoacetate

NH₂

90



(cis-2-Hydrindanylidene)cynoacetamide and

Cynoacetamide

Piperidine

90



(trans-2-Hydrindanylidene)cynoacetamide§ and

Cynoacetamide

Piperidine

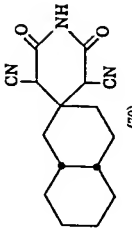
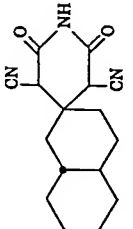
90



Note: References 491-1045 are on pp. 545-555.

† This product was directly condensed further with ethyl bromoacetate or ethyl β-chloropropionate.
 ‡ This compound was formed *in situ* from ethyl cyanoacetate and the corresponding ketone.
 § This compound was formed *in situ* from cyanoacetamide and the corresponding ketone.



TABLE XV—Continued
MICHAEL CONDENSATIONS WITH ALICYCLIC α,β -ETHYLENIC ESTERS

Reactants	Catalyst	Product (Yield, %)	References
<i>Ethyl (cis-2-Decalylidene)cynoacetate and</i>			
Ethyl cyanoacetate	NH ₃	 (70)	944
<i>Ethyl (trans-2-Decalylidene)cynoacetate and</i>			
Ethyl cyanoacetate	NH ₃		944

Note: References 401–1045 are on pp. 545–555.

|| When this compound was formed *in situ* from ethyl cyanoacetate and *trans*-2-decalone, a 60% yield of the same condensation product was obtained.

TABLE XVI
MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENE ESTERS

Reactants	Catalyst	Product (Yield, %)	References
Ethyl (2-Furyl)acrylate and Diethyl malonate	NaOC_2H_5	 (92)	915
Ethyl (4-Pyridyl)acrylate and Diethyl malonate	NaOC_2H_5	 (94)	916
Methyl Cinnamate and Benzyl cyanide Acetophenone	KOCH_3 Dry NaOC_2H_5 NaNH_2	$\text{C}_6\text{H}_5\text{CH}(\text{CH}_2\text{CO}_2\text{CH}_3)\text{CH}(\text{C}_6\text{H}_5)\text{CN}$ (59) $\text{C}_6\text{H}_5\text{CH}(\text{CH}_2\text{CO}_2\text{CH}_3)\text{CH}(\text{C}_6\text{H}_5)\text{CN}$ $\text{C}_6\text{H}_5\text{CH}(\text{CH}_2\text{CO}_2\text{H})\text{CH}(\text{C}_6\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5$ (49)*	83 83 327

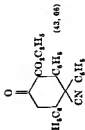
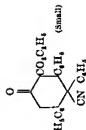
Note: References 491-1045 are on pp. 545-555.

* This product was isolated after hydrolysis.

TABLE XVI—Continued

MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC ESTERS			References
Reactants	Catalyst	Product (Yield, %)	
<i>Ethyl Cinnamate and</i>		$A = C_6H_5CHCH_2CO_2C_2H_5$	
Diethyl malonate†	$NaOC_2H_5$	$ACH(CO_2C_2H_5)_2$ (quant.)	2, 24, 878, 947
Diethyl methylmalonate	$NaOC_2H_5$ (catalyt. amt.) $NaOC_2H_5$ (1 equiv.)	$AC(CH_3)(CO_2C_2H_5)_2$ (50) $C_6H_5CHCH(CH_3)CO_2C_2H_5$ $CH(CO_2C_2H_5)_2$ (Mixture of 2 isomers, 40)	50 50
Ethyl isobutyrate	$NaOC_2H_5$ $(C_6H_5)_3CNa$	$(CH_3)_2C(A)CO_2C_2H_5$ (50)	468
Diethyl succinate	$NaOC_2H_5$	$(CH_3)_2C(A)CO_2C_2H_5$ (20)	468
Ethyl phenylacetate	$NaOC_2H_5$ $(C_6H_5)_3CNa$	2-Phenylbutane-1,3,4-tricarboxylic acid (24)* $C_6H_5CH(A)CO_2C_2H_5$ (quant.)	948
Ethyl acetate†	$(C_6H_5)_3CNa$	$C_6H_5CH(A)CO_2C_2H_5$ (10)	81, 82
Ethyl cyanoacetate	$NaOC_2H_5$	$CH_3COCH(A)CO_2C_2H_5$ (60) $NCCH(A)CO_2C_2H_5$ (two isomers, 85)	468 468
Cyanoacetamide	Na enolate	3-Cyano-2,6-dioxo-4-phenylpiperidine	290, 79, 80, 949
Ethyl α -cyanobutyrate	$NaOC_2H_5$	$NCC(C_2H_5)(A)CO_2C_2H_5$	843
Ethyl α -cyanoisovalerate	$NaOC_2H_5$	$NCC(C_3H_7-i)(A)CO_2C_2H_5$	80
Ethyl α -cyanohydrocinnamate	$NaOC_2H_5$	$NCC(CH_2C_6H_5)(A)CO_2C_2H_5$	80 80

$C_6H_5CH(\Delta)CN$ (Two isomers: 27 total; 50 total; and 27, 83, 952, 84
 32 + 12 or 44 total)
 $C_6H_5CH(\Delta)CN$ (80); $C_6H_5CH(CN)CH(C_6H_5)CH_2CO_2H$
 (Small); 950



Dry $NaOC_2H_5$

83, 952,
951

Note: References 491-1095 are on pp. 545-555.

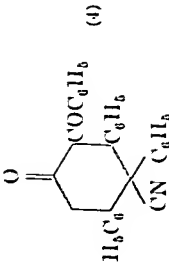
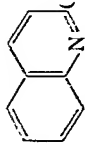
* This product was isolated after hydrolysis.

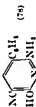
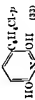

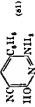
† According to ref. 80, amides of cinnamic acid and cinnamionitrile react analogously. Hydrolysis of the primary condensation product affords, with partial decarboxylation, β -phenylglutaric acid. The primary product from cinnamamide is



‡ Ethyl acetate was used; it was transformed into ethyl acetoacetate before the reaction with ethyl cinnamate.

TABLE XVI—Continued

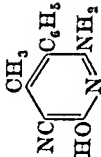
MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC ESTERS			
Reactants	Catalyst	Product (Yield, %)	References
<i>Ethyl Cinnamate (Cont.) and</i>			
Benzyl cyanide (Cont.)	NaOCH_3 Dry NaOH	$\text{A} = \text{C}_6\text{H}_5\text{CHCH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{C}_6\text{H}_5\text{CH}(\text{CN})\text{CH}(\text{C}_6\text{H}_5)\text{CH}_2\text{CO}_2\text{CH}_3$ $\text{C}_6\text{H}_5\text{CH}(\text{A})\text{CN}$ (33); $\text{C}_6\text{H}_5\text{CH}(\text{CN})\text{CH}(\text{C}_6\text{H}_5)\text{CH}_2\text{CO}_2\text{H}$ (35); $\text{C}_6\text{H}_5\text{CH}(\text{A})\text{CONH}_2$ (12)	833 950
γ -Benzyl- α,β -diphenyl- butyronitrile	NaOC_2H_5	 (4)	952
Pinacolone	NaNH_2	$\text{A}(\text{CH}_2)_2\text{COC}(\text{CH}_3)_3$ (64)	327
Acetophenone	NaNH_2	$\text{A}(\text{CH}_2)_2\text{COC}_6\text{H}_5$ (19) or $\text{C}_6\text{H}_5\text{COCCH}_2\text{CH}(\text{C}_6\text{H}_5)\text{CH}_2\text{CO}_2\text{H}$ (37-66)	327, 953
Nitromethane	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OC}_4\text{H}_9$ $[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	$\text{A}(\text{CH}_2)_2\text{NO}_2$ (76) $\text{A}(\text{CH}(\text{NO}_2)\text{CO}_2\text{C}_2\text{H}_5)$ (66)	40 154
2-Quinaldine	—	 (10)*	374
Triethyl phosphononacetate	NaOC_2H_5 ; K	$(\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{O})\text{CH}(\text{A})(\text{CO}_2\text{C}_2\text{H}_5)$ (24, 50)	124, 817
<i>Ethyl 4-Nitrocinnamate and</i> Cyanonacetamide	Na enolate	3-(Cyano-2,6-dioxo-4-(<i>p</i> -nitrophenyl)piperidine	843

<i>Ethyl β-Hydroxyinnamate and</i> $\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	None	6-Hydroxy-2-methyl-4-phenylpyridine-3-carboxylic acid (25)*	954
<i>Ethyl Atropate (α-Phenylacrylate) and</i> Triethyl ethane-1,1,2-carboxylate	NaOC_2H_5	$\text{C}_6\text{H}_5\text{O}_2\text{CCH}(\text{C}_6\text{H}_5)\text{CH}_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)_2\text{CH}_2\text{C}(\text{O}_2\text{C}_2\text{H}_5)_2$	56
<i>Ethyl β-Methoxy α-phenylacrylate and</i> Cyanacetamide	NaOC_2H_5	2,6-Dihydroxy-3-phenylpyridine (28)	955
<i>β-Methoxy-α-phenylacrylonitrile and</i> Cyanacetamide	NaOC_2H_5	 (76)	955
<i>Ethyl β-Ethoxy-α-(p-chlorophenyl)acrylate and</i> Cyanacetamide	NaOC_2H_5	 (32) or  (33)	955
<i>Ethyl β-Isobutyry-α-phenylacrylate and</i> Cyanacetamide	NaOC_2H_5	2,6-Dihydroxy-3-phenylpyridine (31)	955
<i>β-Isobutyry-α-phenylacrylonitrile and</i> Cyanacetamide	NaOC_2H_5	 (31)	955

Note: References 491-1015 are on pp. 545-555.

* This product was isolated after hydrolysis.

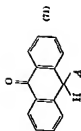
TABLE XVI—Continued

MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC ESTERS			References
Reactants	Catalyst	Product (Yield, %)	
<i>Ethyl p-Methylcinnamate and</i> <i>Ethyl α-cyanopropionate</i>	NaOC_2H_5	$\text{CH}_3\text{C}(\text{CN})(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}(\text{C}_6\text{H}_4\text{CH}_3\text{-}p)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	80
<i>Ethyl α-Methylcinnamate and</i> <i>Ethyl cyanoacetate</i>	NaOC_2H_5	$\text{NCCH}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}(\text{C}_6\text{H}_5)\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$ (Two isomers, 58)	50, 80
<i>Ethyl Hydroxymethylcyclophenylacetate and</i> <i>Malonic acid</i>	None	α -Phenylglutaconic acid (75)*	366
<i>Cyanoacetic acid</i>	None	Ethyl 4-cyano-2-phenyl-2-butenate (47)	366
<i>Ethyl β-Benzylacrylate and</i> <i>Diethyl malonate</i>	Na enolate	$A = \text{C}_6\text{H}_5\text{CH}_2\text{CHCH}_2\text{CO}_2\text{C}_2\text{H}_5$ <div style="text-align: center;"> </div> $\text{ACH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (51) $\text{AC}(\text{CH}_3)(\text{CO}_2\text{C}_2\text{H}_5)_2$ (42) $\text{ACH}(\text{CN})(\text{CO}_2\text{C}_2\text{H}_5)$ (67)	950
<i>Diethyl methylmalonate</i> §	NaOC_2H_5		77
<i>Ethyl cyanoacetate</i> §	NaOC_2H_5		77
<i>β-Isobutyryl-α-phenylcrotononitrile and</i>			
<i>Cyanoacetamide</i>	NaOC_2H_5	 (33)	955
<i>Dimethyl Benzylidenemalonate and</i>			
<i>Isobutyraldehyde</i> <i>Deoxybenzoin</i>	NaOCH_3 NaOCH_3	$A = \text{C}_6\text{H}_5\text{CHCH}(\text{CO}_2\text{CH}_3)_2$ <div style="text-align: center;"> </div> $(\text{CH}_3)_2\text{C}(A)\text{CHO}$ (80) $\text{C}_6\text{H}_5\text{COCH}(A)\text{C}_6\text{H}_5$ (44)	957 163

163

NaOCH₃

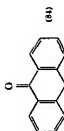
Anthrone



329

NaOCH₃

Nitromethane

*Dimethyl m-Nitrobenzylidenemalonate and*ACH₃NO₂ (95)

958

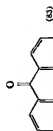
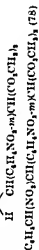
Piperidine

Anthrone

959

NaOCH₃

Phenylnitromethane

Dimethyl o-Chlorobenzylidenemalonate and

960

Piperidine

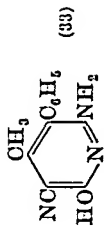
Anthrone

Note. References 491-1045 are on pp. 545-555.

* This product was isolated after hydrolysis.

‡ Instead of ethyl β-benzylacrylate, ethyl styrylacrylate was employed.

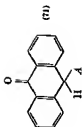
TABLE XVI—Continued

MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC ESTERS			References
Reactants	Catalyst	Product (Yield, %)	
<i>Ethyl p-Methylcinnamate and Ethyl α-cyanopropionate</i>	NaOC_2H_5	$\text{CH}_3\text{C}(\text{CN})(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}(\text{C}_6\text{H}_4\text{CH}_3\text{-}p)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	80
<i>Ethyl α-Methylcinnamate and Ethyl cyanoacetate</i>	NaOC_2H_5	$\text{NCCH}(\text{CO}_2\text{C}_2\text{H}_5)\text{CH}(\text{C}_6\text{H}_5)\text{CH}(\text{CH}_3)\text{CO}_2\text{C}_2\text{H}_5$ (Two isomers, 58)	50, 80
<i>Ethyl Hydroxymethylcyclophenylacetate and Malonic acid</i>	None	α -Phenylglutaconic acid (75)*	300
<i>Cyanoacetic acid</i>	None	Ethyl 4-cyano-2-phenyl-2-butenonate (47)	300
<i>Ethyl β-Benzylacrylate and Diethyl malonate</i>	Na enolate	$\text{A} = \text{C}_6\text{H}_5\text{CH}_2\text{CHCH}_2\text{CO}_2\text{C}_2\text{H}_5$ $\text{A}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (51)	950
<i>Diethyl methylmalonate§</i>	NaOC_2H_5	$\text{A}(\text{CH}_3)(\text{CO}_2\text{C}_2\text{H}_5)_2$ (42)	77
<i>Ethyl cyanoacetate§</i>	NaOC_2H_5	$\text{A}(\text{CN})(\text{CO}_2\text{C}_2\text{H}_5)_2$ (67)	77
<i>β-Isobutyroxy-α-phenylcrotononitrile and Cyanacetamide</i>			
	NaOC_2H_5	 (33)	955
<i>Dimethyl Benzylidenemalonate and Isobutyraldehyde</i>			
	NaOCH_3	$\text{A} = \text{C}_6\text{H}_5\text{CHCH}_2\text{CO}_2\text{CH}_3$ $(\text{CH}_3)_2\text{C}(\text{A})\text{CHO}$ (80)	957
<i>Deoxybenzoin</i>	NaOCH_3	$\text{C}_6\text{H}_5\text{COCH}(\text{A})\text{C}_6\text{H}_5$ (44)	103

163

NaOCH₃

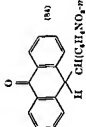
Anthrone



329

NaOCH₃

Nitromethane

*Dimethyl m-Nitrobenzylidenemalonate and*ACH₃NO₂ (85)

958

Piperidine

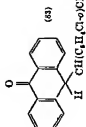
Anthrone

 $\text{C}_6\text{H}_5\text{CH}(\text{NO}_2)\text{CH}(\text{C}_6\text{H}_4\text{NO}_2\text{-}m)\text{CH}(\text{CO}_2\text{CH}_3)_2$ (78)

959

NaOCH₃

Phenylnitromethane

Dimethyl o-Chlorobenzylidenemalonate and

900

Piperidine

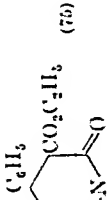
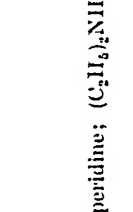
Anthrone

Note: References 491-1045 are on pp. 545-555.

* This product was isolated after hydrolysis.

§ Instead of ethyl β -benzylacrylate, ethyl styrylacrylate was employed.

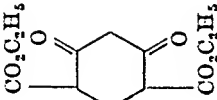
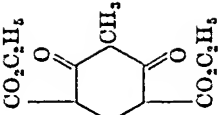
TABLE XVI—Continued

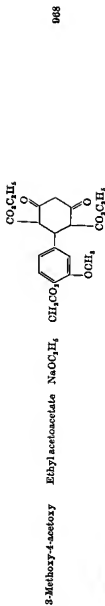
MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC ESTERS			
Reactants	Catalyst	Product (Yield, %)	References
<i>Diethyl Benzylidenemalonate and</i>			
Diethyl malonate	Na enolate	$A\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (quant.)	901
Ethyl acetate	NaOC_2H_5	$\text{CH}_3\text{COCH}(A)\text{CO}_2\text{C}_2\text{H}_5$ (81)	901
$\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	None	 (76)	902, 580, 903
Ethyl isobutyrylacetate	NaOC_2H_5	$(\text{CH}_3)_2\text{CHCOCH}(A)\text{CO}_2\text{C}_2\text{H}_5$ (65)	901
Anthrone	Piperidine; $(\text{C}_2\text{H}_5)_2\text{NH}$	 (71, 91)	40, 900
Deoxybenzoin	NaOC_2H_5	$\text{C}_6\text{H}_5\text{COCH}(A)\text{C}_6\text{H}_5$	416
Phenylnitromethane	$(\text{C}_2\text{H}_5)_2\text{NH}$; NaOC_2H_5	$\text{C}_6\text{H}_5\text{CH}(A)\text{NO}_2$ (80, 52)	29, 905
Ethyl nitronacetate	$(\text{C}_2\text{H}_5)_2\text{NH}$	$\text{ACH}(\text{NO}_2)\text{CO}_2\text{C}_2\text{H}_5$ (90)	20

Substituted Diethyl Benzylidenemalonates					References
Substituent(s) in $C_6H_5CH=C(CO_2C_2H_5)_2$	Addend	Catalyst	Product (Yield, %)		
2-Chloro	Anthrone	Piperidine		(73)	960
3-Nitro	Diethyl malonate	Na enolate	$(C_2H_5O_2C)CHCH(C_6H_4NO_2-3)CH(CO_2C_2H_5)_2$		901
	Anthrone	Piperidine			958
4-Nitro	Nitromethane	$NaOC_2H_5$	$O_2NCH_2CH(C_6H_4NO_2-3)CH(CO_2C_2H_5)_2$		966
	Diethyl malonate	Na enolate	$(C_2H_5O_2C)CHCH(C_6H_4NO_2-4)CH(CO_2C_2H_5)_2$		901
	Nitromethane	$NaOC_2H_5$	$O_2NCH_2CH(C_6H_4NO_2-4)CH(CO_2C_2H_5)_2$		966
4-Methoxy	Deoxybenzoin	$NaOC_2H_5$	$C_6H_5COCH(C_6H_5)CH(C_6H_4OCH_3-4)CH(CO_2C_2H_5)_2$		416
4-Dimethylamino	Deoxybenzoin	$NaOC_2H_5$	$C_6H_5COCH(C_6H_5)CH[C_6H_4N(CH_3)_2-4]CH(CO_2C_2H_5)_2$		416
3,4-Methylenedioxy	Deoxybenzoin	$NaOC_2H_5$	$C_6H_5COCH(C_6H_5)CH[C_6H_3(O_2CH)_2-3,4]CH(CO_2C_2H_5)_2$		416

Note: References 491-1045 are on pp. 545-555.

TABLE XVI—Continued
MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC ESTERS
Substituted Diethyl Benzylidenemalonates—Continued

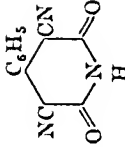
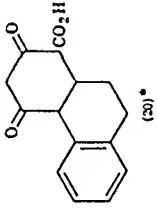
Substituent(s) in $C_6H_5CH=C(CO_2C_2H_5)_2$	Addend	Catalyst	Product (Yield, %)	References
4-Acetoxy	Ethyl acetoacetate	$NaOC_2H_5$	 $4-CH_3CO_2C_2H_5$	957
Ethyl propionyl- acetate	$NaOC_2H_5$	$p-CH_3CO_2C_2H_5$	 $p-CH_3CO_2C_2H_5$	428





Reactants	Catalyst	Product (Yield, %)	References
<i>Ethyl Benzylidenecyanoacetate and</i>			
Ethyl cyanoacetate	$(\text{C}_2\text{H}_5)_3\text{NH}$	 (Diethylammonium salt, 80)	969
$\text{C}_6\text{H}_5\text{C}(=\text{NH})\text{CH}_2\text{CN}$	$(\text{C}_2\text{H}_5)_3\text{NH}$	3,5 Dicyano-4,6-diphenyl-2-piperidone (5)	331
<i>Ethyl (α-Phenylethylidene)cyanoacetate and</i>			
Ethyl acetoacetate	NaOC_2H_5		415

Note: References 491-1045 are on pp. 545-555.

TABLE XVI—Continued

MICHAEL CONDENSATIONS WITH AROMATIC α,β -ETHYLENIC ESTERS		References
Reactants	Product (Yield, %)	
<i>Benzylidenecyanoacetamide and Cyanoacetamide</i>		
Catalyst		
KOH	$C_6H_5CH_2CH(CN)CONH_2$ or $C_6H_5CH=C(CN)CONH_2$	896
		
<i>Ethyl Cinnamylidenacetate and Diethyl malonate</i>	β -Styrylglutaric acid (38)*	194, 195
<i>Ethyl 3,4-Dihydropyrophosphate and Ethyl acetoneacetate</i>		970
<i>Ethyl 4-Phenyl-2-pentenolate and Ethyl cyanacetate</i>	$C_6H_5CH(CH_3)CH(CH_2CO_2C_2H_5)CH(CN)CO_2C_2H_5$ (50)	77

<i>Diethyl 3-Pyridylmethylmalonate and</i> <i>Phenylformethane</i>	$(C_5H_4)_2NH$		29
<i>Ethyl nitroacetate</i>	$(C_2H_5)_2NH$		29
<i>Dimethyl Cinnamylidenemalonate and</i> <i>Dimethyl malonate</i> <i>Nitromethane</i>	$NaOCH_3$ $NaOCH_3$	$C_6H_5CH[CH(CO_2CH_3)_2]CH_2CH[CH(CO_2CH_3)_2] $ $C_6H_5CH=CHCH(CH_2NO_2)CH(CO_2CH_3)_2$ (87)	56, 971 329
<i>Diethyl Benzylidenesuccinate and</i> <i>Diethyl malonate</i>	KOC_2H_5	2-Phenylbutane-1,1,3,4-tetracarboxylic acid,* 2-phenylbutane-1,3,4-tricarboxylic acid*	948
<i>Ethyl α-Cyano-γ,γ-diphenylgluteronate and</i> <i>Ethyl cyanacetate</i> [†]	$(C_2H_5)_2NH$	β-Benzhydrylglutaric acid* (12-21)	972


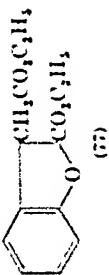
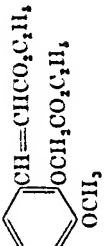
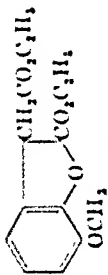

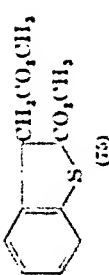
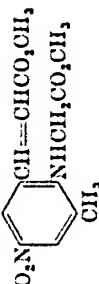
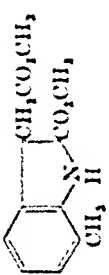

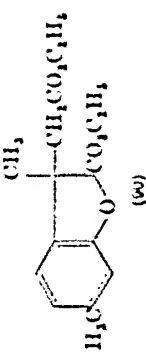
Note: References 491-1045 are on pp. 545-555.

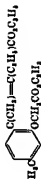
* This product was isolated after hydrolysis.

† This is the formula of the expected condensation product; in fact, a pentamethyl ester was isolated. This same product is obtained in 97% yield when cinnamaldehyde and dimethyl malonate are condensed in the presence of sodium methoxide.

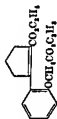
‡ The unsaturated ester was formed *in situ* from diphenylacetaldehyde and ethyl cyanoacetate.

TABLE XVI
INTRAMOLECULAR MICHAEL CONDENSATIONS OF AROMATIC α,β -ETHYLENIC ESTERS

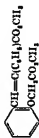
Reactant	Catalyst	Product (Yield, %)	References
	NaOC2H5	 (57)	974, 973
	NaOC2H5	 (58)	973
	NaOCH3	 (59)	332
	NaOCH3	 (60)	332
	NaOC2H5	 (60)	973, 974

NaOC₂H₅

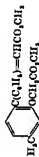
974

NaOC₂H₅

974, 973

NaOCH₃

332

NaOCH₃

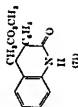
332

NaOC₂H₅

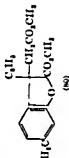
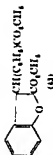
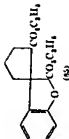
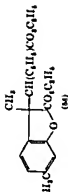
974

NaOCH₃

332



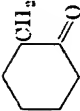
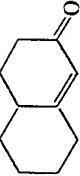
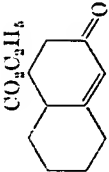
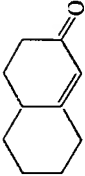
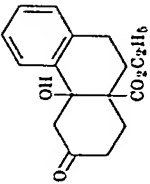
Note: References 491-1045 are on pp. 545-555.



(71)

TABLE XVII

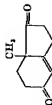
MICHAEL REACTIONS WITH α,β -ETHYLENIC KETO ESTERS

Reactants	Catalyst	Product (Yield, %)	References
<i>Sodium Methyleneacetate</i> * and 2-Carboxycyclohexanone	NaOH	 and 	528
2-Carboethoxycyclohexanone	NaOH	 and 	528
2-Methylcyclopentane-1,3-dione 2-Methylcyclohexane-1,3-dione	NaOH, piperidine NaOH	8-Hydroxy-9-methylhydriindane-3,6-dione 2-(β -Acetyl-ethyl)-2-methylcyclohexane-1,3-dione	528 528
<i>Ethyl Methyleneacetate</i> † and Ethyl acetate	NaOH, sec-amine NaOH	4-Carboethoxy-3-methyl-2-cyclohexen-1-one 10-Carboethoxy-2-oxo-2,3,4,5,6,7,8,10-octahydronaphthalene	528 528
2-Carboethoxy-1-tetralone	NaOH		528
2-Formyl-1-cyclohexanone	NaOH	2-(β -Acetyl- β -carboethoxyethyl)-2-formylcyclohexanone (37)	528

Sodium Methylencediacetonedicarboxylate† and

2-Methylcyclopentane-1,3-dione NaOH

528



2-Methylcyclohexane-1,3-dione NaOH

528

Ethyl α -(Aminomethylene)acetacetate and

Ethyl acetacetate

None

Acetone

None

Cyclohexanone

None

Diethyl 2,6-dimethylpyridine-3,5-dicarboxylate (30)

120

Ethyl 2,5,6-trimethylpyridine-3-carboxylate (8)

120

Ethyl 2-methyl-5,6,7,8-tetrahydroquinoline-3-carboxylate
(20-30)

120

Ethyl β -Acetylacrylate and

Diethyl malonate

NaOC₂H₅CH₃COCH₂CH(CO₂C₂H₅)CH(CO₂C₂H₅)₂

975

Ethyl β -Acetyl- α -hydroxyacrylate (Acetylpyruvate) and

Cyanoacetamide

NH₂; (C₂H₅)₂NH

Piperidine

NaOCH₃K₂CO₃

None

4-Carboxy-3-cyano-6-methyl-2-pyridone

371

4-Carboxy-3-cyano-6-methyl-2-pyridone (15)

976

4-Carboxy-3-cyano-6-methyl-2-pyridone (65)

976

4-Carboxy-3-cyano 6-methyl-2-pyridone (82)

976, 977

Diethyl 2,6-dimethylpyridine-3,4-dicarboxylate (80)

978, 979

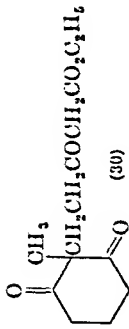
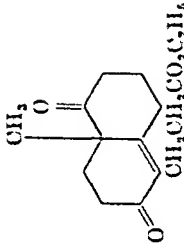
Note: References 491-1045 are on pp. 545-555.


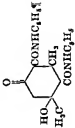
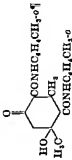
* A mixture of sodium acetacetate and formaldehyde was employed.

† A mixture of ethyl acetacetate and formaldehyde was employed.

‡ A mixture of sodium acetonedicarboxylate and formaldehyde was employed.

TABLE XVII—Continued

MICHAEL REACTIONS WITH α,β -ETHYLENIC KETO ESTERS			References
Reactants	Catalyst	Product (Yield, %)	
<i>Ethyl β-Acetyl-α-ethoxyacrylate and Cynnonacetamide</i>	K_2CO_3	2-Carboethoxy-5-cyano-4-methyl-6-pyridone (73)	90
<i>Ethyl 3-Oxo-4-pentenolate and</i>			
2-Methylcyclohexane-1,3-dione	$NaOCH_3$	 (30)	538
<i>Ethyl α-Acetyl-β-hydroxyacetate (Diethylacetalate) and Cynnonacetamide</i>	Pyridine	3-Cyano-4-methyl-6-hydroxy-2-pyridone §	308
<i>Methyl 5-Oxo-6-heptenolate and</i>			
2-Methylcyclohexane-1,3-dione	$NaOCH_3$	 (58)	538
<i>Ethyl β-Propionyl-α-hydroxyacrylate (Propionylpyruvate) and Cynnonacetamide</i>	Piperidine	Ethyl 3-cyano-6-ethyl-2-hydroxypyridine-4-carboxylate (58)	980

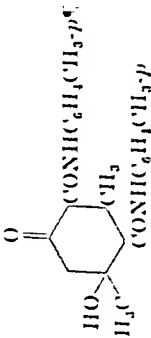

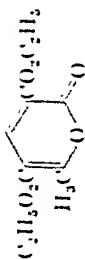
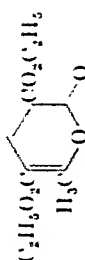
<i>Ethyl α-Ethylideneacetoacetate and Ethyl acetoacetate</i>	Diethyl α,α'-diacetyl-β-methylglutarate (93)	981, 982, 983
1-Tetralone		206
<i>Ethylideneacetoacetanilide and Acetoacetanilide</i>	$\text{CH}_3\text{CH}[\text{CH}(\text{COCH}_3)\text{CONHC}_6\text{H}_5]_2$ (50) $\text{CH}_3\text{CH}[\text{CH}(\text{COCH}_3)\text{CONHC}_6\text{H}_5]_2$ (60)	984 984
<i>Ethylideneacetoacet-o-toluide and</i>		984
<i>Acetoacet-o-toluide</i>		984

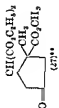
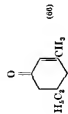
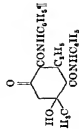
Note: References 491-1045 are on pp. 545-555.

§ Ethyl acetate is eliminated in this reaction.

|| The ethylenic compound was formed *in situ* from the corresponding aldehyde and the keto acid derivative.
¶ This product is formed when the reaction is carried out in boiling pyridine.

TABLE XVII—Continued
MICHAEL REACTIONS WITH α,β -ETHYLENIC KETO ESTERS

Reactants	Catalyst	Product (Yield, %)	References
<i>Ethylidenecoumarate-p-toluide and Acetoned-p-toluide</i>	None	$\text{C}_6\text{H}_5\text{CH}(\text{CH}(\text{COCH}_3))\text{CONHC}_6\text{H}_4\text{CH}_3\text{-}p^2$	984
<i>Ethyl α-Methoxymethylcinnacoumarate and Cyanomacetamide</i>	Pyridine NaOC_2H_5		984
<i>Ethyl α-Ethoxymethylcinnacoumarate and Cyanomacetamide</i>	NaOC_2H_5		330
<i>Ethyl α-Ethoxymethylcinnacoumarate and Diethyl malonate</i>	NaOC_2H_5		310
<i>Ethyl cyanomacetate</i>	NaOC_2H_5		310
<i>Ethyl β-n-Butyryl-α-hydroxycinnerylate (n-Butyrylphenacrylate) and Cyanomacetamide</i>	Piperidine	Ethyl 3-cyano-2-hydroxy-6-propylpyridino-4-carboxylate (51)	985

<i>Ethyl β-Isobutyryl-α-hydroxyacrylate (Isobutyrylpyruvate) and Cyanoacetamide</i>	K ₂ CO ₃	Ethyl 3 cyano-2-hydroxy-6-isopropylpyridine-4-carboxy-Late (70)	977
<i>4 Carbomethoxy-3-methyl 2-cyclohexen-1-one and Diethyl malonate</i>	Na enolate		986
<i>Ethyl α-Propylidenecouacetate and Ethyl acetacetate</i>	NaOC ₂ H ₅ ; (C ₂ H ₅) ₂ NH	Diethyl α,α'-diacetyl β ethylglutarate	982, 983, 986a
<i>α-Propylidenecouacetamide and Acetacetamide</i>	Pyridine		982
	None	C ₂ H ₅ CH[CH(COCH ₃)CONHC ₂ H ₅] ₂	981
	Pyridine		981

Note: References 491-1045 are on pp. 545-555.

|| The ethylene compound was formed *in situ* from the corresponding aldehyde and the keto acid derivative.

† This product is formed when the reaction is carried out in boiling pyridine.

** This is the structure assumed by the authors.

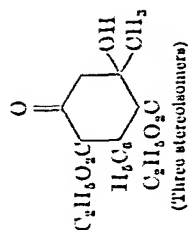
TABLE XVII—Continued
MICHAEL REACTIONS WITH α,β -ETHYLENIC KETO ESTERS

Reactants	Catalyst	Product (Yield, %)	References
<i>Ethyl (2-Keto-3-methylcyclohexyl)glyoxalate and</i> $\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	None	Diethyl 2,8-dimethyl-9-hydroxy-5,6,7,8,9,10-hexahydro-quinoline-3,4-dicarboxylate	952
<i>Ethyl (2-Keto-4-methylcyclohexyl)glyoxalate and</i> $\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	None	Diethyl 2,7-dimethyl-9-hydroxy-5,6,7,8,9,10-hexahydro-quinoline-3,4-dicarboxylate	952
<i>Ethyl (2-Keto-5-methylcyclohexyl)glyoxalate and</i> $\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	None	Diethyl 2,6-dimethyl-9-hydroxy-5,6,7,8,9,10-hexahydro-quinoline-3,4-dicarboxylate	952
<i>Ethyl Methylcyclohexylacetate and</i> Ethyl benzoylacetate	$(\text{C}_2\text{H}_5)_2\text{NH}$	$\text{CH}_2[\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)(\text{C}_6\text{H}_5)_2]$	992
<i>Ethyl β-Benzoyl-α-hydroxyacrylate (Benzoylpyruvate) and</i> Cyanocetamide	Piperidine	Ethyl 3-cyano-2-hydroxy-6-phenylpyridine-4-carboxylate (30)	977
<i>Ethyl γ-Benzylidenacetate and</i> Dooxybenzoin	NaOC_2H_5	3,4,5-Triphenyl-2-cyclohexen-1-one	993

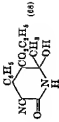
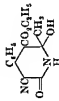
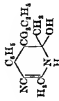
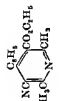
Ethyl α -Benzylidenacetate and

Ethyl acetoacetate||

Piperidine



982

Ethyl cyanacetate	$(C_2H_5)_3NH$	 (68)	969
	Aq. $(C_4H_9)_3NH$	$C_2H_5O_2COH(COCH_3)CH(C_4H_9)CH(CN)CONH_2$;	969
			
$CH_3C(=NH)CH_2CN$	$(C_4H_9)_3NH$	 or 	440
$C_4H_5C(=NH)CH_2CN$	$NaOCH_3$	Ethyl 5-cyano-4,6-diphenyl-2-methylpyridine-3-carboxylate††	331
$p-CH_3C_6H_4C(=NH)CH_2CN$	$NaOCH_3$	Ethyl 5-cyano-2-methyl-4-phenyl-6-p-tolylpyridine-3-carboxylate	331
$p-CH_3OC_6H_4C(=NH)CH_2CN$	$NaOCH_3$	Ethyl 5-cyano-6-p-methoxyphenyl 2-methyl-4-phenylpyridine-3-carboxylate	331
Phenylacetalddehyde	$NaOC_2H_5$	$C_6H_5CH[CH(C_2H_5)CHO]CH(COCH_3)CO_2C_2H_5$ (36)	163

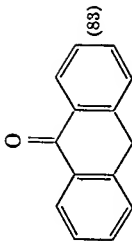
Note: References 491-1013 are on pp. 545-555.

|| The ethylenic compound was formed *in situ* from the corresponding aldehyde and the keto acid derivative.

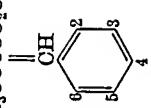
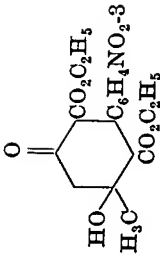
†† By self-condensation, part of the $C_6H_5C(=NH)CH_2CN$ is converted into 3,5-dicyano-2,4,6-triphenylidihydropyridine.

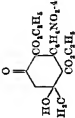
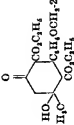
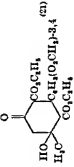
TABLE XVII—Continued

MICHAEL REACTIONS WITH α,β -ETHYLENIC KETO ESTERS

Reactants	Catalyst	Product (Yield, %)	References
<i>Ethyl α-Benzylidenecoacetate (Cont.) and</i>			
Anthrone	NaOC_2H_5	 (83)	163
Phenylnitromethane	$(\text{C}_2\text{H}_5)_2\text{NH}$	3-Carbethoxy-5-nitro-4,5-diphenyl-2-pentanone (78)	29

Substituted Ethyl α -Benzylidenecoacetates

Substituent(s) in $\text{CH}_3\text{COCO}_2\text{C}_2\text{H}_5$	Addend	Catalyst	Product (Yield, %)	References
				
3-Nitro	Ethyl acetoacetate	Piperidine		982, 994

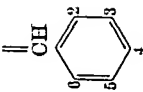
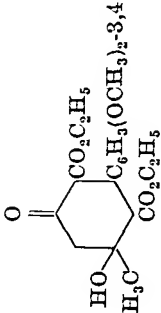
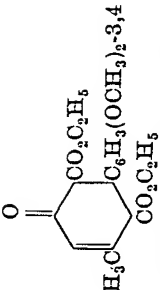
Deoxybenzoin	NaOC_2H_5	$3\text{-O}_2\text{N}_2\text{C}_6\text{H}_4\text{CHCH}(\text{COCH}_3)\text{CO}_2\text{C}_2\text{H}_5$ $\quad \quad \quad $ $\quad \quad \quad \text{C}_6\text{H}_5\text{CHCOC}_2\text{H}_5$	416
4-Nitro	Ethyl acetoacetate Piperidine		982, 994
2-Methoxy	Ethyl acetoacetate NaOC_2H_5		982; cf. 995
3-Cyano 4-Cyano	Ethyl acetoacetate Pyridine Ethyl acetoacetate Pyridine	3-NCC ₆ H ₄ CH(CH(COCH ₃))CO ₂ C ₂ H ₅ (77) 4-NCC ₆ H ₄ CH(CH(COCH ₃))CO ₂ C ₂ H ₅ (77)	996 996
3,4-Methylenedioxy	Ethyl acetoacetate $\{\text{C}_6\text{H}_4\text{CH}_2\text{N}(\text{CH}_3)_2\}\text{OH}$		536


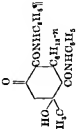
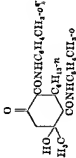
Note: References 491-1015 are on pp. 545-555.

|| The ethylenic compound was formed *in situ* from the corresponding aldehyde and the keto acid derivative.

TABLE XVII—Continued

MICHAEL REACTIONS WITH α,β -ETHYLENIC KETO ESTERSSubstituted Ethyl α -Benzylidenacetates—Continued

Substituent(s) in $\text{CH}_3\text{COCO}_2\text{C}_2\text{H}_5$	Addend	Catalyst	Product (Yield, %)	References
	Ethyl acetate	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	 (14)	536
			 (Mixtures of stereoisomers, 34)	

Reactants	Catalyst	Product (Yield, %)	References
<i>Ethyl α-n-Heptylidenacetate and Ethyl acetoacetate</i>	NaOC_2H_5 ; $(\text{C}_2\text{H}_5)_3\text{NH}$	Diethyl α,α' -diacetyl- β -n-hexylglutarate	990
<i>α-n-Heptylidenacetanilide</i> and Acetoacetanilide	Piperidine None	 $n\text{-H}_{13}\text{C}_4$	981
<i>α-n-Heptylidenacetate</i> and Acetoacetanilide	Pyridine	$n\text{-C}_6\text{H}_{13}\text{CH}[\text{CH}(\text{CONHC}_6\text{H}_5)\text{CONHC}_6\text{H}_5]_2$	984
<i>α-n-Heptylidenacetate</i> and Acetoacet-o-toluide	Pyridine		984
<i>Acetoacet-o-toluide</i>	Pyridine		984

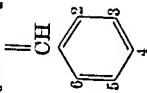
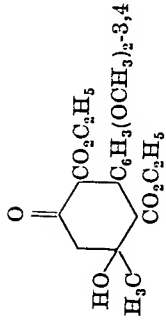
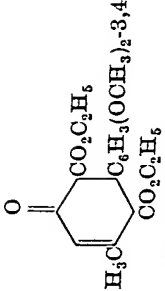
Note: References 491-1045 are on pp. 545-555


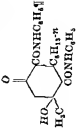
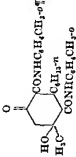
|| The ethylenic compound was formed *in situ* from the corresponding aldehyde and the keto acid derivative.

¶ This product is formed when the reaction is carried out in boiling pyridine.

TABLE XVII—Continued

MICHAEL REACTIONS WITH α,β -ETHYLENIC KETO ESTERS*Substituted Ethyl α -Benzylidenacetates—Continued*

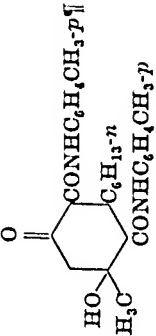
Substituent(s) in $\text{CH}_3\text{COCO}_2\text{C}_2\text{H}_5$	Addend	Catalyst	Product (Yield, %)	References
$\text{CH}=\text{C}_6\text{H}_4$ 	Ethyl acetonediacetate	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	 (14)	536
3,4-Dimethoxy			 (Mixtures of stereoisomers, 34)	

Reactants	Catalyst	Product (Yield, %)	References
<i>Ethyl α-n-Heptylidenecarboxylate and Ethyl acetoacetate</i>	NaOC_2H_5 ; $(\text{C}_2\text{H}_5)_3\text{NH}$	<i>Diethyl α,α'-diacetyl-β-n-hexylglutarate</i>	990
	Piperidine		981
<i>α-n-Heptylidenecarboxaldehyde</i> and <i>Acetoacetanilide</i>	None	$n\text{-C}_6\text{H}_{13}\text{CH}[\text{CH}(\text{COCH}_3)\text{CONHC}_6\text{H}_5]_2$	984
	Pyridine		984
<i>α-n-Heptylidenecarboxylate-o-toluide</i> and			
<i>Acetoacet-o-toluide</i>	Pyridine		984

Note: References 491-1045 are on pp. 545-555.

|| The ethylenic compound was formed *in situ* from the corresponding aldehyde and the keto acid derivative.
 ¶ This product is formed when the reaction is carried out in boiling pyridine.

TABLE XVII—Continued

MICHAEL REACTIONS WITH α,β -ETHYLENIC KETO ESTERS			
Reactants	Catalyst	Product (Yield, %)	References
α - <i>n</i> -Heptylideneacetacet- <i>p</i> -toluide and Acetoacet- <i>p</i> -toluide	Pyridine		984
Ethyl β -Cinnamoyl- α -hydroxyacrylate (Cinnamoylpyruvate) and $\text{CH}_3\text{C}(=\text{NH})\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	None	Diethyl 2-methyl-6-styrylpyridine-3,4-dicarboxylate (48)	954
Ethyl α -Benzylidenemalonate and Diethyl malonate	NaOC_2H_5	$\text{C}_6\text{H}_5\text{CHCH}(\text{CO}_2\text{C}_2\text{H}_5)\text{COCH}(\text{CH}_3)_2$ $\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (72)	964
Ethyl Citrylideneacetacetate and Ethyl acetoacetate	Piperidine	Diethyl citrylidene-bis-acetoacetate (61)	997
Ethyl Benzylidenemalonate and Phenylnitromethane	$(\text{C}_2\text{H}_5)_2\text{NH}$	Ethyl α -benzoyl- γ -nitro- β,γ -diphenylbutyrate (71)	20



Note: References 491–1045 are on pp. 545–555.

|| The ethylenic compound was formed *in situ* from the corresponding aldehyde and the keto acid derivative.

¶ This product is formed when the reaction is carried out in boiling pyridine.

TABLE XVIII

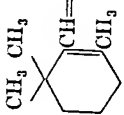
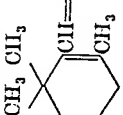
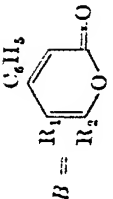
MICHAEL CONDENSATIONS WITH α,β -ACETYLENIC ESTERS

Reactants	Catalyst	Product (Yield, %)	References
<i>Methyl Propiolate and</i> 1-Tetralone	NaNH_2 , liq. NH_3	Methyl 1-tetralone-2-acrylate*	998
<i>Ethyl Propiolate and</i> Diethyl methylmalonate Ethyl acetoacetate	Na NaOC_2H_5	$A = -\text{CH}=\text{CHCO}_2\text{C}_2\text{H}_5$ $\text{CH}_3\text{C}(\Delta)(\text{CO}_2\text{C}_2\text{H}_5)_2$ (14) $\text{CH}_3\text{COCH}(A)\text{CO}_2\text{C}_2\text{H}_5$	333 999
6-Methoxy-1-tetralone	NaNH_2 , liq. NH_3		998
1-Keto-1,2,3,4-tetrahydronaphthalene	NaNH_2 , liq. NH_3	 (34)	998
α -Phenylbutyronitrile	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	$\text{CH}_3\text{CH}_2\text{C}(\text{C}_6\text{H}_5)(A)\text{CN}$ (35)	1000

Note: References 491-1045 are on pp. 545-555.

* The product was directly reduced to methyl 1-tetralone-2-propionate.

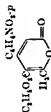
TABLE XVIII—Continued
MICHAEL CONDENSATIONS WITH α,β -ACETYLENIC ESTERS

Reactants	Catalyst	Product (Yield, %)	References
<i>Ethyl Propiolate (Cont.) and</i> γ -Diethylamino- α -phenylbutyronitrile	$[(C_6H_5CH_2N-(CH_3)_3)OH]$	$A = -CH=CHCO_2C_2H_5$ $(C_2H_5)_2NCH_2CH_2C(C_6H_5)(A)CN$ (59)	1000
Diphenylacetoneitrile	$[C_6H_5CH_2N-(CH_3)_3]OH$	$(C_6H_5)_2C(A)CN$ (92)	1000
<i>Ethyl Tetrolate and</i> Diethyl malonate	$NaOC_2H_5$	$A = CH_3C=CHCO_2C_2H_5$ $A CH(CO_2C_2H_5)_2$	109, 1001, 1002
		$CH=CHC(CH_3)=CHCOC(A)(CO_2C_2H_5)_2$	1003, 1004
<i>Tetrolonitrile and</i> 	$NaOC_2H_5$	$CH=CHC(CH_3)=CHCOC(CO_2C_2H_5)_2$ $CH_3C=CHCN$	1003
<i>Ethyl Phenylpropiolate and</i> Diethyl malonate	$Na, NaOC_2H_5$	$A = C_6H_5C=CHCO_2C_2H_5$ $A CH(CO_2C_2H_5)_2$	25, 20, 878, 1005
		 R_1, R_2	

Diethyl methylmalonate	Na; NaOC ₂ H ₅	β -Phenylglutaconic acid†	1006, 1007, 1008, 333, 25, 20, cf. 334
Diethyl benzylmalonate	NaOC ₂ H ₅	Cl ₂ C(A)(CO ₂ C ₂ H ₅) ₂ (14)	431
Ethyl acetoacetate	NaOC ₂ H ₅	C ₆ H ₅ CH ₂ C(A)(CO ₂ C ₂ H ₅) ₂	430, 431
Ethyl <i>n</i> -propylacetoacetate	NaOC ₂ H ₅	B, R ₁ = CO ₂ C ₂ H ₅ , R ₂ = CH ₃ (14)	433
Ethyl oxaloacetate	NaOC ₂ H ₅	CH ₂ COC(A)(C ₂ H ₅)- α -CO ₂ C ₂ H ₅	433
Ethyl benzoylacetate	NaOC ₂ H ₅	B, R ₁ = R ₂ = CO ₂ C ₂ H ₅	431
Ethyl cyanoacetate	Na	B, R ₁ = CO ₂ C ₂ H ₅ , R ₂ = C ₆ H ₅	25
Acetylacetone	NaOC ₂ H ₅	N(CCH(A)CO ₂ C ₂ H ₅) ₂	432
Benzoylacetone	NaOC ₂ H ₅	CH ₂ COCCH(A)COCCH ₃ ; B, R ₁ = COCH ₃ , R ₂ = CH ₃	433
Deoxybenzoin	NaOC ₂ H ₅	B, R ₁ = H, R ₂ = CH ₃	432, 433
Ethyl fluorene-9-carboxylate	Na enolate	B, R ₁ = COCH ₃ , R ₂ = C ₆ H ₅	1009
		Ethyl β -(9-fluorenyl)cinnamate (28)	1010

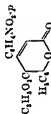
Ethyl *p*-Nitrophenylpropionate and

Ethyl acetoacetate

NaOC₂H₅

433

Ethyl benzoylacetate

NaOC₂H₅

433

Note: References 491-1045 are on pp. 545-555.

† This product results from hydrolysis and partial decarboxylation.

TABLE XVIII—Continued
MICHAEL CONDENSATIONS WITH α,β -ACETYLENIC ESTERS

Reactants	Catalyst	Product (Yield, %)	References
<i>Ethyl 2,3-Dimethoxyphenylpropionate and Ethyl acetate</i>	NaOC_2H_5	5-Carboethoxy-4-(2',3'-dimethoxyphenyl)-6-methyl- α -pyrone (71)	1011
Acetylacetone	NaOC_2H_5	2,3-(CH_3O) ₂ $\text{C}_6\text{H}_3\text{C}=\text{CHCO}_2\text{C}_2\text{H}_5$ $\text{CH}_3\text{COC}=\text{C}(\text{OH})\text{CH}_3$ (33);	1011
<i>2,3-Dimethoxyphenylpropionitrile and Acetylacetone</i>	NaOC_2H_5	2,3-(CH_3O) ₂ $\text{C}_6\text{H}_3\text{C}=\text{CHCN}$ $\text{CH}_3\text{COC}=\text{C}(\text{OH})\text{CH}_3$ (43);	1011
<i>Diethyl Acetylenedicarboxylate and Diethyl malonate</i>	Na	$\text{A} = \text{C}_2\text{H}_5\text{O}_2\text{CCH}=\text{CCO}_2\text{C}_2\text{H}_5$ 	333
Diethyl methylmalonate	$\text{Na}; \text{NaOC}_2\text{H}_5$	$\text{ACH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (30)	333
Triethyl ethane-1,1,2-tricarboxylate	NaOC_2H_5	$\text{CH}_3\text{C}(\text{A})(\text{CO}_2\text{C}_2\text{H}_5)_2$	325
Tetraethyl ethane-1,1,2,2-tetracarboxylate	NaOC_2H_5	Pentaethyl 1-butene-1,2,3,3,4-pentacarboxylate Hexaethyl 1-butene-1,2,3,3,4,4-hexacarboxylate (16)§	325, 480
Ethyl acetate	NaOC_2H_5	$\text{CH}_3\text{COCH}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$	433, 1012
Ethyl benzoylacetate	NaOC_2H_5	$\text{C}_6\text{H}_5\text{COCH}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$	433, 1012


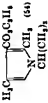
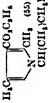
Note: References 491–1045 are on pp. 545–555.

+ The free acid corresponding to this product was actually isolated.

§ Originally (ref. 489), this product was assumed to be a cyclobutane derivative, formed by a second, intramolecular, Michael reaction. The cyclobutane structure has now been disproved (ref. 325).

TABLE XIX

MICHAEL CONDENSATIONS WITH α,β -ETHYLENIC NITRO COMPOUNDS

Reactants	Catalyst	Product (Yield, %)	References
1-Nitro-1-propene and Ethyl acetoacetate	NaOC_2H_5	$\text{O}_2\text{NCH}_2\text{CH}(\text{CH}_3)\text{CH}(\text{COCH}_3)\text{CO}_2\text{C}_2\text{H}_5$ (31)	1013
$\text{CH}_3\text{C}(=\text{NCH}_3)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	None		1013
$\text{CH}_3\text{C}(=\text{NCH}(\text{CH}_3)_2)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	None		1013
$\text{CH}_3\text{C}(=\text{NCH}(\text{CH}_3)\text{CH}_2\text{NO}_2)\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5$	None		1013
2-Nitro-1-propene and 2-Nitropropane Methyl 2-nitropropyl ether Methyl 2-nitropropyl sulfide	NaOC_2H_5 NaOC_2H_5 NaOCH_3	$A = \text{CH}_2\text{CH}(\text{NO}_2)\text{CH}_2-$ $\text{AC}(\text{CH}_3)_2\text{NO}_2$ (20) $\text{AC}(\text{NO}_2)(\text{CH}_3)\text{CH}_2\text{OCH}_3$ (50) $\text{AC}(\text{NO}_2)(\text{CH}_3)\text{CH}_2\text{SCH}_3$ (30)	1014 1014 1014

Notes: References 491-1045 are on pp. 545-555.

TABLE XIX—Continued
MICHAEL CONDENSATIONS WITH α,β -ETHYLENIC NITRO COMPOUNDS

Reactants	Catalyst	Product (Yield, %)	References
<i>Nitromalonalddehyde (Hydroxymethylenitroacetaldehyde) and</i>			
Ethyl acetoacetate	Alkali	5-Nitrosalicylic acid	111
Cyanoacetamide	$[\text{C}_6\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_3]\text{OH}$	3-Cyano-5-nitro-2-pyridone (93)	111
Levulinic acid	Alkali	2-Hydroxy-5-nitrophenylacetic acid (82)	111
Acetonedicarboxylic acid	Alkali	2-Hydroxy-5-nitrobenzene-1,3-dicarboxylic acid	111
Acetone	Alkali	<i>p</i> -Nitrophenol	339
Methyl ethyl ketone	Alkali	2-Methyl-4-nitrophenol (90)	111
Acetonylacetone	Alkali	Methyl 2-hydroxy-5-nitrobenzyl ketone, 2,2'-dihydroxy-5,5'-dinitrobiphenyl	1015, 1016 111, 340,
Methyl benzyl ketone	Alkali	2-Hydroxy-5-nitrobiphenyl	341
Dibenzyl ketone	Alkali	2,6-Diphenyl-4-nitrophenol (94)	111, 340, 341
Cycloöctanone	Na enolate	2,6-Pentamethylene-4-nitrophenol* (10)	342, 343
Cyclononanone	Na enolate	2,6-Hexamethylene-4-nitrophenol (62)	342
Cyclodecanone	Na enolate	2,6-Heptamethylene-4-nitrophenol (6)	342
Cycloundecanone	Na enolate	2,6-Octamethylene-4-nitrophenol (2)	343
Cyclododecanone	Na enolate	2,6-Nonamethylene-4-nitrophenol (28)	342
Cyclotridecanone	Na enolate	2,6-Decamethylene-4-nitrophenol (70)	342
Cyclotetradecanone	Na enolate	2,6-Undecamethylene-4-nitrophenol (64)	342
Cyclopentadecanone	Na enolate	2,6-Dodecamethylene-4-nitrophenol (74)	342
Cyclohexadecanone	Na enolate	2,6-Tridecamethylene-4-nitrophenol (63)	342
Cycloheptadecanone	Na enolate	2,6-Tetradecamethylene-4-nitrophenol (57)	342
Cycloöctadecanone	Na enolate	2,6-Pentadecamethylene-4-nitrophenol (40)	342
Cyclononadecanone	Na enolate	2,6-Hexadecamethylene-4-nitrophenol (43)	343

Cycloicosanone	Na enolate	2,6-Heptadecamethylene-4-nitrophenol (47)	342
Cycloleneicosanone	Na enolate	2,6-Octadecamethylene-4-nitrophenol (16)	342
Cyclotriacontanone	Na enolate	2,6-Heptacosamethylene-4-nitrophenol	342
1-Nitro-1-butene and		$A = \text{CH}_2\text{CH}_2\text{CHCH}_2\text{NO}_2$	
Ethyl α -propylacetoacetate	Na	$\text{CH}_3\text{COC}(A)(\text{C}_2\text{H}_5)_2\text{CO}_2\text{C}_2\text{H}_5$	1017
Ethyl α -cyanobutyrate	NaOC_2H_5	$\text{CH}_3\text{CH}_2\text{C}(\text{CN})(A)\text{CO}_2\text{C}_2\text{H}_5$	1018
Benzyl cyanide†	KOC_2H_5	$\text{C}_6\text{H}_5\text{CH}(A)\text{CN}$	1018
Acetylacetone	Na	$\text{CH}_3\text{COCH}(A)\text{COCH}_3$ (30)	1019
2-Nitro-1-butene and		$A = \text{CH}_2\text{CH}_2\text{CH}(\text{NO}_2)\text{CH}_2-$	
Diethyl malonate	NaOC_2H_5	$\text{ACH}(\text{CO}_2\text{C}_2\text{H}_5)_2$	1020†
Diethyl phenylmalonate	NaOC_2H_5	$\text{C}_6\text{H}_5\text{C}(A)(\text{CO}_2\text{C}_2\text{H}_5)_2$ (13)	1020
Ethyl acetoacetate	Na	$\text{CH}_3\text{COCH}(A)\text{CO}_2\text{C}_2\text{H}_5$ (25)	1017
Methyl cyanoacetate‡	None	$\text{ACH}(\text{CN})\text{CO}_2\text{CH}_3$ (23)	1021
Ethyl cyanoacetate	NaOC_2H_5	$\text{ACH}(\text{CN})\text{CO}_2\text{C}_2\text{H}_5$ (16 crude)	1018, 1021
1-Nitropropane	NaOH	$\text{CH}_3\text{CH}_2\text{CH}(A)\text{NO}_2$ (18)	1021
2-Nitropropane¶	NaOH	$(\text{CH}_3)_2\text{C}(A)\text{NO}_2$ (55)	1021
Acetylacetone	Na	$\text{CH}_3\text{COCH}(A)\text{COCH}_3$	1019

Note: References 491-1045 are on pp. 545-555.

* Chemical Abstracts name: 9-Nitrobicyclo[5.3.1]hendeca-1(11),4,9-triene-11-ol.



† Instead of 1-nitro-1-butene, β -nitroisopropyl acetate was employed.

‡ In this patent, a number of similar products of Michael condensations are mentioned.

§ 1-Dimethylamino-2-nitrobutane was employed instead of 2-nitro-1-butene.

|| Instead of 2-nitro-1-butene, 1-diethylamino-2-nitrobutane was used. When the corresponding 1-dimethylamino compound was employed, the yield was somewhat higher.

¶ Instead of 2-nitro-1-butene, 1-dimethylamino-2-nitrobutane was employed.

1-Nitro-1-pentene and Diethyl malonate	Na	$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_2\text{NO}_2)\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (95)	1020
3,3,4,4,5,5-Hexafluoro-1-nitro-1-pentene and Nitromethane Diethyl malonate	NaOCH_3 NaOC_2H_5	$ \begin{array}{c} \text{A} = \text{CF}_3\text{CF}_2\text{CF}_2\text{CHCH}_2\text{NO}_2 \\ \\ \text{A} \text{CH}_2\text{NO}_2 \text{ (68)} \\ \text{A} \text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2 \text{ (54)} \end{array} $	863 863
3-Nitro-3-hexene and Diethyl malonate	NaOC_2H_5	$\text{CH}_3\text{CH}_2\text{CH}(\text{NO}_2)\text{CH}(\text{C}_2\text{H}_5)\text{CH}(\text{CO}_2\text{C}_2\text{H}_5)_2$	1020
Ethyl α -Nitro- γ,γ -trichloroacrylate and Ethyl nitroacetate	$(\text{C}_2\text{H}_5)_3\text{NH}$	$\text{Cl}_3\text{CCH}(\text{CH}(\text{NO}_2)\text{CO}_2\text{C}_2\text{H}_5)_2$ (34)	1024
1-Nitrocyclohexene and <i>p</i> -Bromobenzyl cyanide	$\text{KOC}_2\text{H}_{11}$, ⁴	 (Mixture of isomers, 8)	85
2-Nitropropane	NaOC_2H_5	 (16)	1014

Note: References 491-1015 are on pp. 545-555.

TABLE XIX—Continued
MICHAEL CONDENSATIONS WITH α,β -ETHYLENIC NITRO COMPOUNDS

Reactants	Catalyst	Product (Yield, %)	References
<i>Methyl 2-Nitro-2-pentenolate and</i>		$A = \text{CH}_3\text{CH}_2\text{CH}(\text{NO}_2)\text{CO}_2\text{CH}_3$	
1,1-Dinitroethane	NaOH, aq. CH_3OH	$\text{AC}(\text{NO}_2)_2\text{CH}_3$ (61)	813
Methyl 2,2-dinitrobutyrate	Na derivative, water	$(\text{NO}_2)_2\text{C}(\text{A})\text{CH}_2\text{CH}_2\text{CO}_2\text{CH}_3$	813
1-(α -Furyl)-2-nitroethylene and Ethyl nitroacetate	$(\text{C}_2\text{H}_5)_2\text{NH}$	Ethyl 3-(α -furyl)-2,4-dinitrobutanoate (95)	622
<i>ω-Nitrostyrene and</i>		$A = \text{C}_6\text{H}_5\text{CH}(\text{CH}_3)\text{NO}_2$	
Dimethyl malonate	Na	$\text{ACH}(\text{CO}_2\text{CH}_3)_2$	329
Diethyl malonate	NaOC_2H_5	$\text{ACH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (51)	1025
Ethyl acetacetate	Na; $(\text{C}_2\text{H}_5)_3\text{N}$	$\text{CH}_3\text{COCH}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (98)	1017, 1025
Ethyl benzoylacetate	Na	$\text{C}_6\text{H}_5\text{COCH}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$	1017
Acetylacetone	Na, $(\text{C}_2\text{H}_5)_3\text{N}$	$\text{CH}_3\text{COCH}(\text{A})\text{COCH}_3$ (78)	1019, 1025
Benzoylacetone	$(\text{C}_2\text{H}_5)_3\text{N}$	$\text{C}_6\text{H}_5\text{COCH}(\text{A})\text{COCH}_3$ (86)	1025
Ethyl nitroacetate	$(\text{C}_2\text{H}_5)_2\text{NH}$	$\text{ACH}(\text{NO}_2)\text{CO}_2\text{C}_2\text{H}_5$ (97)*	151
Phenylnitromethane	$(\text{C}_2\text{H}_5)_2\text{NH}$	$\text{C}_6\text{H}_5\text{CH}(\text{A})\text{NO}_2$ (91)	622
<i>α-Nitrostyrene and</i>		$A = o\text{-O}_2\text{NC}_6\text{H}_4\text{CH}_2\text{CH}_3$	
Dimethyl malonate	NaOCH_3	$\text{ACH}(\text{CO}_2\text{CH}_3)_2$ (49); $(\text{A})_2\text{C}(\text{CO}_2\text{CH}_3)_2$ (2)	314
Diethyl malonate	NaOC_2H_5	$\text{ACH}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (72)	314
Diethyl ethylmalonate	NaOC_2H_5	$\text{C}_2\text{H}_5\text{C}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (41)	314
Methyl acetacetate	NaOCH_3	$\text{CH}_3\text{COCH}(\text{A})\text{CO}_2\text{CH}_3$ (32)	314

Ethyl acetoacetate	NaOC ₂ H ₅	CH ₃ COCH(A)CO ₂ C ₂ H ₅ (42)	344
Ethyl n-butylacetoacetate	NaOC ₂ H ₅	CH ₃ COC(C ₄ H ₉) _n (A)CO ₂ C ₂ H ₅ (61)	344
Methyl cyanoacetate	NaOCH ₃	ACH(CN)CO ₂ CH ₃ (69)	344
Ethyl cyanoacetate	NaOC ₂ H ₅	ACH(CN)CO ₂ C ₂ H ₅ (78)	344
Cyanoacetamide	NaOC ₂ H ₅	(A) ₂ C(CN)CONH ₂ (42)	344
<i>p</i> -Nitrostyrene and			
Dimethyl malonate	NaOCH ₃	A = <i>p</i> -O ₂ NC ₆ H ₄ CH ₂ CH ₃ —	
Diethyl malonate	NaOC ₂ H ₅	ACH(CO ₂ CH ₃) ₂ (43), (A) ₂ C(CO ₂ CH ₃) ₂ (32)	344
Diethyl ethylmalonate	NaOC ₂ H ₅	ACH(CO ₂ C ₂ H ₅) ₂ (45), (A) ₂ C(CO ₂ C ₂ H ₅) ₂ (34)	344
Methyl acetoacetate	NaOCH ₃	AC(C ₂ H ₅)/CO ₂ C ₂ H ₅ (56)	344
Ethyl acetoacetate	NaOC ₂ H ₅	CH ₃ COCH(A)CO ₂ CH ₃ (38), CH ₃ COC(A) ₂ CO ₂ CH ₃ (24)	344
		CH ₃ COCH(A)CO ₂ C ₂ H ₅ (47), CH ₃ COC(A) ₂ CO ₂ C ₂ H ₅ (19)	344
Ethyl n-butylacetoacetate	NaOC ₂ H ₅	CH ₃ COC(C ₂ H ₅) _n (A)CO ₂ C ₂ H ₅ (57)	344
Methyl cyanoacetate	NaOCH ₃	(A) ₂ C(CN)CO ₂ CH ₃ (79)	344
Ethyl cyanoacetate	NaOC ₂ H ₅	(A) ₂ C(CN)CO ₂ C ₂ H ₅ (80)	344
Cyanoacetamide	NaOC ₂ H ₅	(A) ₂ C(CN)CONH ₂ (73)	344
Malononitrile	NaOC ₂ H ₅	(A) ₂ C(CN) ₂ (36)	344
<i>β</i> -Methyl- <i>β</i> -nitrostyrene and			
Diethyl malonate	Na enolate	Diethyl 3-nitro-2-phenylbutane-1,1-dicarboxylate (79)†††	86




Note: References 491-1015 are on pp. 545-555.

** The product was isolated as the *ac*-diethylammonium salt.

†† In ether as solvent, only one of the two diastereomerides is formed; in alcohol a mixture of the two is obtained.

‡‡ When the reaction product is worked up with acid, this compound is transformed into 1,1-dicarbethoxy-2-phenylbutan-3-one.

TABLE XIX—Continued

MICHAEL CONDENSATIONS WITH α,β -ETHYLENIC NITRO COMPOUNDS			
Reactants	Catalyst	Product (Yield, %)	References
<i>Ethyl β-(2-Furyl)-α-nitroacrylate</i> §§ and Ethyl nitroacetate	$(C_2H_5)_2NH$	 $CH[CH(NO_2)CO_2C_2H_5]_2$ (83, 85)**	154, 1024
<i>Ethyl α-Nitro-β-(2-pyridyl)acrylate</i> §§ and Ethyl nitroacetate	$(C_2H_5)_2NH$	 $CH[CH(NO_2)CO_2C_2H_5]_2$ (82, 84)**	154, 1024
<i>Ethyl α-Nitro-β-(3-pyridyl)acrylate</i> §§ and Ethyl nitroacetate	$(C_2H_5)_2NH$	 $CH[CH(NO_2)CO_2C_2H_5]_2$ (55)**	154
<i>Methyl α-Nitrocinnamate</i> §§ and Methyl nitroacetate	CH_3NH_2 ; $(C_2H_5)_2NH$	$C_6H_5CH[CH(NO_2)CO_2CH_3]_2$ (70)	1024
<i>Ethyl α-Nitrocinnamate</i> and Diethyl malonate	$(C_2H_5)_2NH$	$A = C_6H_5CHCH(NO_2)CO_2C_2H_5$ 3,3-Dicarbethoxy-1-nitro-2-phenylbutyric acid diethylamide (82)	1020
Ethyl acetacetate	$(C_2H_5)_2NH$	$CH_3COCH(A)CO_2C_2H_5$ (85)	1020
Benzyl cyanide	$(C_2H_5)_2NH$	$C_6H_5CH(A)CN$ (83)	1020
Ethyl nitroacetate§§	$(C_2H_5)_2NH$	$ACH(NO_2)CO_2C_2H_5$ (80, 84-88, 74)**	154, 1024, 1020
Phenyl nitromethane	$(C_2H_5)_2NH$	$C_6H_5CH(A)NO_2$ (82)	1020


<i>Ethyl</i> α ,2-Dinitrocinname §§ and Ethyl nitroacetate	(C ₂ H ₅) ₂ NH	2-O ₂ NC ₂ H ₄ CH[CH(NO ₂)CO ₂ C ₂ H ₅] ₂ (82, 68)**	154, 1024
<i>Ethyl</i> α ,3-Dinitrocinname §§ and Ethyl nitroacetate	(C ₂ H ₅) ₂ NH	3-O ₂ NC ₂ H ₄ CH[CH(NO ₂)CO ₂ C ₂ H ₅] ₂ (90-95, 66)**	154, 1024
<i>Ethyl</i> α ,4-Dinitrocinname and Ethyl acetoacetate	(C ₂ H ₅) ₂ NH	CH ₃ COCH(CO ₂ C ₂ H ₅)CH(C ₂ H ₄ NO ₂) ₂ CH(NO ₂)CO ₂ C ₂ H ₅ (85)	1026
Ethyl nitroacetate §§	(C ₂ H ₅) ₂ NH	4-O ₂ NC ₂ H ₄ CH[CH(NO ₂)CO ₂ C ₂ H ₅] ₂ (82, 60, 38)**	154, 1024, 1026
<i>Ethyl</i> 2-Hydroxy- α -nitrocinname §§ and Ethyl nitroacetate	(C ₂ H ₅) ₂ NH	2-HOC ₂ H ₄ CH[CH(NO ₂)CO ₂ C ₂ H ₅] ₂ (90, 98)**	154, 1024
<i>Ethyl</i> 4-Hydroxy- α -nitrocinname §§ and Ethyl nitroacetate	(C ₂ H ₅) ₂ NH	4-HOC ₂ H ₄ CH[CH(NO ₂)CO ₂ C ₂ H ₅] ₂ (84)**	154
<i>Ethyl</i> 2-Chloro- α -nitrocinname §§ and Ethyl nitroacetate	(C ₂ H ₅) ₂ NH	2-ClC ₂ H ₄ CH[CH(NO ₂)CO ₂ C ₂ H ₅] ₂ (97)**	154, 1024
<i>Ethyl</i> 4-Chloro- α -nitrocinname and Ethyl acetoacetate	(C ₂ H ₅) ₂ NH	CH ₃ COCH(CO ₂ C ₂ H ₅)CH(C ₂ H ₄ Cl) ₂ CH(NO ₂)CO ₂ C ₂ H ₅ , (85)	1026
Ethyl cyanoacetate	(C ₂ H ₅) ₂ NH	NCCH(CO ₂ C ₂ H ₅)CH(C ₂ H ₄ Cl) ₂ CH(NO ₂)CO ₂ C ₂ H ₅ , (85)	1026
Ethyl nitroacetate §§	(C ₂ H ₅) ₂ NH	4-ClC ₂ H ₄ CH[CH(NO ₂)CO ₂ C ₂ H ₅] ₂ (97)**	154, 1024

Note: References 491-1045 are on pp. 545-555.

** The product was isolated as the *aci*-diethylammonium salt.

§§ The unsaturated ester was formed *in situ* from the ester of nitroacetic acid and the appropriate aldehyde.

TABLE XIX—Continued

MICHAEL CONDENSATIONS WITH α,β -ETHYLENIC NITRO COMPOUNDS			
Reactants	Catalyst	Product (Yield, %)	References
<i>Ethyl 4-Methoxy-α-nitrocinnamate</i> §§ and Ethyl nitroacetate	$(C_2H_5)_2NH$	4-CH ₃ OC ₆ H ₄ CH[CH(NO ₂)(CO ₂ C ₂ H ₅) ₂] (72)••	151
<i>Ethyl β-Methyl-α-nitrocinnamate</i> §§ and Ethyl nitroacetate	$[C_2H_5CH_2N(CH_3)_2]OC_4H_9$, <i>n</i>	Diethyl 1,3-dinitro-2-methyl-2-phenylglutarate (70)	151
<i>Ethyl Cyclohexyldienitroacetate</i> and Ethyl nitroacetate	$[C_2H_5CH_2N(CH_3)_2]OC_4H_9$, <i>n</i>	<div style="text-align: center;">  (61) </div>	154
<i>Ethyl α-Nitro-β-propylacrylate</i> §§ and Ethyl nitroacetate	$(C_2H_5)_2NH$	Diethyl 1,3-dinitro-2- <i>n</i> -propylglutarate (95)••	622
<i>Ethyl β-Isopropyl-α-nitroacrylate</i> §§ and Ethyl nitroacetate	$(C_2H_5)_2NH$	Diethyl 1,3-dinitro-2-isopropylglutarate••	622
<i>Ethyl β-Isobutyl-α-nitroacrylate</i> §§ and Ethyl nitroacetate	$(C_2H_5)_2NH$	Diethyl 1,3-dinitro-2-isobutylglutarate (90)••	622
2-Nitro-2-phenyl-1-(3'-pyridyl)ethylene†,† and Phenyltrimethane	CH ₃ NH ₂	1,3-Dinitro-1,3-diphenyl-2-(3'-pyridyl)propane (48)	29

α -Nitrostilbene and		$A = C_6H_5CHCH(NO_2)C_6H_5$	
Dimethyl malonate	NaOCH ₃	ACH(CO ₂ CH ₃) ₂ (85)	965
Diethyl malonate	NaOC ₂ H ₅	ACH(CO ₂ C ₂ H ₅) ₂ (29)	29, 903
		ACH(CO ₂ C ₂ H ₅) ₂ (two isomers, 87)***	86
Ethyl acetoacetate	NaOC ₂ H ₅	CH ₃ COCH(A)CO ₂ C ₂ H ₅ (42)	29
Ethyl cyanoacetate	NaOC ₂ H ₅	C ₆ H ₅ CH ₂ NO ₂ and C ₆ H ₅ CH=C(CN)CO ₂ C ₂ H ₅ (60)	29
Acetylacetone	NaOC ₂ H ₅	CH ₃ COCH(A)COCH ₃ (11)	29
Phenylacetone	NaOC ₂ H ₅	C ₆ H ₅ CH(A)COCH ₃ (13); C ₆ H ₅ CH ₂ NO ₂ and C ₆ H ₅ CH=C(C ₆ H ₅)COCH ₃	29
Benzoylacetone	NaOC ₂ H ₅	C ₆ H ₅ COCH(A)COCH ₃ (21)	29
Phenylnitromethane†††	CH ₃ NH ₂	C ₆ H ₅ CH(A)NO ₂ ; 1-nitro-1,2,3-triphenyl-1-propene; 3,4,5-triphenylisoxazole	1027
3-Nitro-1,4-diphenyl-3-buten-1-one and			
Dimethyl malonate	NaOCH ₃	C ₆ H ₅ COCH ₂ CH(NO ₂)CH(C ₆ H ₅)CH(CO ₂ CH ₃) ₂ (65)†††	1028

Note: References 491-1045 are on pp. 545-555.

** The product was isolated as the *act*-diethylammonium salt.

§§ The unsaturated ester was formed *in situ* from the ester of nitroacetic acid and the appropriate aldehyde.

||| The unsaturated ester was formed *in situ* from ethyl nitroacetate and the appropriate ketone.

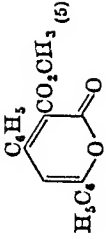
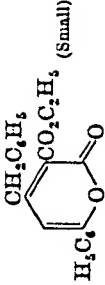
¶¶ This compound was formed *in situ* from pyridine-3-carboxaldehyde and phenylnitromethane.

*** Upon separation of the two isomers, yields of 47 and 17%, respectively, of the pure compounds were obtained.

†† This reaction takes place when benzaldehyde and phenylnitromethane are condensed in the presence of methylamine.

††† This product is obtained at -20°; at -50°, a 30% yield of C₆H₅CH[OH(CO₂CH₃)₂]CH=CHCOC₂H₅ is obtained, and at -33° 10% of an unidentified product, C₁₀H₁₁NO₄, which gives the same 2,4-dinitrophenylhydrazone as the products obtained at the lower temperature.

TABLE XIX—Continued
MICHAEL CONDENSATIONS WITH α,β -ETHYLENIC NITRO COMPOUNDS

Reactant	Catalyst	Product (Yield, %)	References
β -Nitrobenzylidenemalacetophenone and Dimethyl malonate	NaOCH_3		1029
$\text{C}_6\text{H}_5\text{COCH}=\text{C}(\text{NO}_2)\text{CH}_2\text{C}_6\text{H}_5$ and Diethyl malonate	NaOCH_3	<p>or</p> $\text{C}_6\text{H}_5\text{CH}=\text{C}[\text{CH}(\text{CO}_2\text{CH}_3)_2]\text{COC}_6\text{H}_5$ (20)	1029
			1029

Note: References 491–1045 are on pp. 545–555.

TABLE XX

MICHAEL CONDENSATIONS WITH α,β -ETHYLENIC SULFONES

Reactants	Catalyst	Product (Yield, %)	References
<i>Methyl Vinyl Sulfone and</i>		$A = \text{CH}_3\text{SO}_2\text{CH}_2\text{CH}_3$ —	
Diethyl malonate	$[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	$(A)_2\text{C}(\text{CO}_2\text{C}_2\text{H}_5)_2$ (61)	118
Diethyl phenylmalonate	$[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	$\text{AC}(\text{C}_6\text{H}_5)(\text{CO}_2\text{C}_2\text{H}_5)_2$ (58)	118
Ethyl acetoacetate	$[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	$\text{CH}_3\text{COC}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (70)	118
Ethyl cyanoacetate	$[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	$\text{NCC}(\text{A})\text{CO}_2\text{C}_2\text{H}_5$ (81)	118
Benzyl cyanide	$[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	$\text{NCC}(\text{A})_2\text{C}_2\text{H}_5$ (68)	118
Acetylacetone	$[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	$\text{CH}_2\text{COC}(\text{A})\text{COCH}_3$ (36), $\text{CH}_3\text{COCH}(\text{A})_2$ (24)	118
Phenylacetone	$[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	$\text{C}_6\text{H}_5\text{CH}(\text{A})\text{COCH}_3$ (61)	118
Nitromethane	Aq. KOH	$(A)_2\text{CNO}_2$ (50)	1030
p-Bromophenylnitromethane	$[\text{CH}_3\text{N}(\text{C}_2\text{H}_5)_2]\text{OH}$	$p\text{-BrC}_6\text{H}_4\text{CH}(\text{A})\text{NO}_2$ (50)	1030
Phenacyl p-tolyl sulfone	$[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	$\text{C}_6\text{H}_5\text{COCH}(\text{A})\text{SO}_2\text{C}_2\text{H}_5\text{CH}_3$ (61)	118
Diethanesulfonylmethane	$[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	$(A)_2\text{C}(\text{SO}_2\text{C}_2\text{H}_5)_2$ (82)	118
Diethanesulfonylmethane	$[\text{C}_2\text{H}_5\text{CH}_2\text{N}(\text{CH}_3)_2]\text{OH}$	$(A)_2\text{C}(\text{SO}_2\text{CH}_3)_2$ (84)	118
<i>Vinyl n-Butyl Sulfone and</i>		$A = n\text{-C}_4\text{H}_9\text{SO}_2\text{CH}_2\text{CH}_3$ —	
Nitroethane	Aq. NaOH	$\text{ACH}(\text{CH}_3)\text{NO}_2$ (45), $(A)_2\text{C}(\text{CH}_3)\text{NO}_2$ (13)	1030
1-Nitropropane	Aq. KOH	$(A)_2\text{C}(\text{CH}_3)\text{NO}_2$ (75)	1030
	Aq. NaOH	$\text{ACH}(\text{C}_2\text{H}_5)\text{NO}_2$ and $\text{ACH}(\text{C}_2\text{H}_5)\text{NO}_2$ (16)	1030
<i>Vinyl Isobutyl Sulfone and</i>			
p-Bromophenylnitromethane	NaOH	$i\text{-C}_4\text{H}_9\text{SO}_2\text{CH}_2\text{CH}_2\text{CH}(\text{NO}_2)\text{C}_6\text{H}_4\text{Br}$ (30)	1030
<i>Divinyl Sulfone and</i>			
2-Nitropropane	Aq. KOH	$\text{O}_2\text{S}(\text{CH}_2\text{CH}_2\text{C}(\text{CH}_3)_2\text{NO}_2)_2$	1030

Note: References 491-1045 are on pp. 545-555.




TABLE XX—Continued
MICHAEL CONDENSATIONS WITH α,β -ETHYLENIC SULFONES

Reactants	Catalyst	Product (Yield, %)	References
<i>Vinyl p-Tolyl Sulfone and</i> Nitromethane 1-Nitropropane 2-Nitropropane	NaOCH ₃ Aq. KOH Aq. KOH	$A = p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{CH}_2\text{CH}_2\text{—}$ (A) ₂ CHNO ₂ (91) (A) ₂ C(C ₂ H ₅)NO ₂ (CH ₃) ₂ C(A)NO ₂	1031 1030 1030
<i>Phenyl Styryl Sulfone and</i> Diethyl malonate	Na	C ₆ H ₅ SO ₂ CH ₂ CH(C ₆ H ₅)CH(CO ₂ C ₂ H ₅) ₂ (97)	1031
<i>p-Tolyl Styryl Sulfone and</i> Diethyl malonate	Na	$p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{CH}_2\text{CH(C}_6\text{H}_5\text{)CH(CO}_2\text{C}_2\text{H}_5\text{)}_2$ (quant.)	1032
<i>Distyryl Sulfone and</i> Diethyl malonate	Na	O ₂ S[CH ₂ CH(C ₆ H ₅)CH(CO ₂ C ₂ H ₅) ₂] ₂ (74) $A = \text{CH}_2\text{CH}_2\text{SO}_2\text{N(C}_2\text{H}_5\text{)C}_6\text{H}_5$	1033
<i>Vinylsulfonic Acid N-Ethylanilide and</i> Nitromethane Nitroethane 1-Nitropropane 2-Nitropropane	KOH, CH ₃ OH Excess KOH, CH ₃ OH KOH, CH ₃ OH KOH, CH ₃ OH KOH, CH ₃ OH	(A) ₂ CNO ₂ (38-48) (A) ₂ CHNO ₂ (18) (A) ₂ C(NO ₂)CH ₃ (18-61), ACH(NO ₂)CH ₃ (31-44) (A) ₂ C(NO ₂)CH ₂ CH ₃ (31), ACH(NO ₂)CH ₂ CH ₃ (35-40) (CH ₃) ₂ C(A)NO ₂ (83)	358 358 358 358 358
<i>Vinyl dimethylsulfonium Bromide and</i> Diethyl malonate Methyl acetacetate	Aq. NaOH Aq. NaOH	3,3-Dicarbethoxypropyl dimethylsulfonium salt (48) (3-Acetyl-1-3-carbomethoxypropyl) dimethylsulfonium bromide (68)	22 22

Note: References 491-1045 are on pp. 545-555.

TABLE XXI

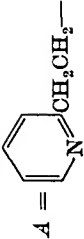
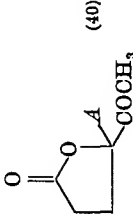
MICHAEL CONDENSATIONS WITH 2- AND 4-VINYLPYRIDINE, WITH ANALOGS OF 2-VINYLPYRIDINE,
AND WITH DITHYL VINYLPHOSPHONATE



A. 2-Vinylpyridine		
Donor	Catalyst	Product (Yield, %)
		
		$A =$
Diethyl malonate	Na NaOC ₂ H ₅	ACH(CO ₂ C ₂ H ₅) ₂ (53) ACH(CO ₂ C ₂ H ₅) ₂ (84, 42-43, 62)
Diethyl ethylmalonate	Na	(A) ₂ C(CO ₂ C ₂ H ₅) ₂ (42-43)
Diethyl isobutyrate	Na	AC(C ₂ H ₅)(CO ₂ C ₂ H ₅) ₂ (39)
Diethyl phenylacetate	Na [C ₆ H ₅ CH ₂ N(CH ₃) ₂]OH	(CH ₃) ₂ C(A)(CO ₂ C ₂ H ₅) (48) C ₂ H ₅ CH(A)(CO ₂ C ₂ H ₅)
Diethyl 2-pyridylacetate	NaOC ₂ H ₅	 (41, 81)
Diethyl acetoacetate	Na, NaOC ₂ H ₅	CH ₃ COCH(A)CO ₂ C ₂ H ₅ (58, 50)
Diethyl n-butylacetoacetate	Na	CH ₃ COC(C ₄ H ₉) _n (A)CO ₂ C ₂ H ₅ (3)
2-Carboethoxycyclopentanone	Na	 (42)

Note: References 491-1045 on are pp. 545-555.

TABLE XXI—Continued

A. 2-Vinylpyridine—Continued


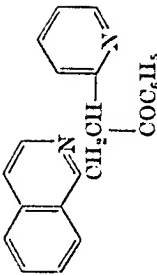
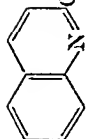
Donor	Catalyst	Product (Yield, %)	References
			
Ethyl benzoylacetate	Na [C ₆ H ₅ CH ₂ N(CH ₃) ₃]OH	C ₆ H ₅ COCH(A)CO ₂ C ₂ H ₅ (70) C ₆ H ₅ COCH(A)CO ₂ C ₂ H ₅	480 1038
γ-Acetyl-γ-butyrolactone	Na		490
Ethyl cyanoacetate	Na	4CH(CN)CO ₂ C ₂ H ₅ (48)	798
Propionitrile	Na	CH ₃ CH(A)CN (19); CH ₃ C(A) ₂ CN (39)	1038
Benzyl cyanide	Na	C ₆ H ₅ CH(A)CN (77)	798
Methyl ethyl ketone	None [C ₆ H ₅ CH ₂ N(CH ₃) ₃]OH Na	CH ₃ CH(A)COCH ₃ CH ₃ CH(A)COCH ₃ (53), CH ₃ C(A) ₂ COCH ₃ (31) CH ₃ COCH(A)CH ₃ (71), CH ₃ COC(A) ₂ CH ₃ (31), 4CH ₂ COC(A) ₂ CH ₃ (16)	1042 1038 1038
Diethyl ketone	Na	CH ₃ CH ₂ COCH(A)CH ₃ (53), CH ₃ CH ₂ COC(A) ₂ CH ₃ (32)	1038
Acetylacetone	NaOC ₂ H ₅	CH ₃ COCH(A)COCH ₃ (16), CH ₃ COC(A) ₂ COCH ₃ (7)	1035
Methyl isopropyl ketone	Na	CH ₃ COC(A)(CH ₃) ₂ (65), 4CH ₂ COC(A)(CH ₃) ₂ (31), (A) ₂ CHCOC(A)(CH ₃) ₂ (39)	1038
Methyl isobutyl ketone	Na	CH ₃ COCH(A)CH(CH ₃) ₂ (20) CH ₃ COC(A) ₂ CH(CH ₃) ₂ (34), 4CH ₂ COC(A) ₂ CH(CH ₃) ₂ (13)	1038

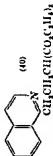
Diisopropyl ketone	Na	$(\text{CH}_3)_2\text{CHCOCH(A)}(\text{CH}_3)_2$ (72), $(\text{CH}_3)_2\text{C(A)}\text{COC(A)}(\text{CH}_3)_2$ (5)	1038
Methyl n-amyl ketone	Na	$\text{CH}_3\text{COCH(A)}\text{C}_4\text{H}_9$ (39), $\text{CH}_3\text{COC(A)}_2\text{C}_4\text{H}_9$ (19)	1038
Dusobutyl ketone	Na	$\text{CH}_3\text{COCH(A)}\text{C}_4\text{H}_9$ (3)	1038
	Na	$(\text{CH}_3)_2\text{CHCH}_2\text{COC(A)}\text{CH}(\text{CH}_3)_2$ (63), $(\text{CH}_3)_2\text{CHCH}_2\text{COC(A)}_2\text{CH}(\text{CH}_3)_2$ (14)	1038
2,5,6-Trimethyl-4-hepten-3-one*	Na	$(\text{CH}_3)_2\text{C(A)}\text{COCH}=\text{C}(\text{CH}_3)\text{CH}(\text{CH}_3)_2$ (29)	1038
Acetophenone	Na	$\text{C}_6\text{H}_5\text{COCH}_2\text{A}$ (8), $\text{C}_6\text{H}_5\text{COCH(A)}_2$ (53)	1038
Phenylacetone	Na	$\text{C}_6\text{H}_5\text{COCH}_2\text{A}$ (11)	1041
	NaOC_2H_5	$\text{CH}_3\text{COCH(A)}\text{C}_6\text{H}_5$ (32)	1038
Propiophenone	Na	$\text{CH}_3\text{COCH(A)}\text{C}_6\text{H}_5$ (44)	1038
	Na	$\text{C}_6\text{H}_5\text{COCH(A)}\text{CH}_3$ (43), $\text{C}_6\text{H}_5\text{COC(A)}_2\text{CH}_3$ (45)	1038
Deoxybenzoin	Na	$\text{C}_6\text{H}_5\text{COCH(A)}\text{CH}_2$ (59)	1038
	NaOC_2H_5	$\text{C}_6\text{H}_5\text{COCH(A)}\text{C}_2\text{H}_5$ (46)	1041
2-Acetylfuran	Na	 (5)	1038
2-Picoline	Na	1,3-Di-(α -pyridyl)propane (33)	454
4-Hydroxycoumarin	Na	 (44)	490

Note: References 491-1045 are on pp. 545-555.

* This ketone was formed and reacted when methyl isopropyl ketone was brought together with sodium metal and 2-vinylpyridine.

TABLE XXI—Continued

A. 2-Vinylpyridine—Continued			References
Donor	Catalyst	Product (Yield, %)	
3-Methyl-4-hydroxycoumarin	Na	 (90)	490
1-Cyano-2-benzoyl-1,2-dihydro- isoquinoline	Li salt	 (50)	805a
B. 4-Vinylpyridine			
Ethyl benzoylacetate	Na	1-Benzoyl-3-(<i>γ</i> -pyridyl)propane (51)†	1041
<i>γ</i> -Picoline	K	1,3-Di-(<i>γ</i> -pyridyl)propane (44)	484
C. Analogs of 2-Vinylpyridine			
Reactants			
2-Vinylquinoline ⁴ and		A =	
Diethyl malonate	NaOC ₂ H ₅	4CH(CO ₂ C ₂ H ₅) ₂ (43)	1043
Ethyl acetoacetate	NaOC ₂ H ₅	CH ₃ COCH(A)CO ₂ C ₂ H ₅ (44)	1043
Ethyl benzoylacetate	NaOC ₂ H ₅	C ₆ H ₅ COCH(A)CO ₂ C ₂ H ₅ (33)	1043

D. Diethyl Vinylphosphonate¹⁰⁴⁵Catalyst NaOC₂H₅A = (C₂H₅O)₂P(O)CH₂CH₂—

Donor	Product (Yield, %)
Diethyl malonate	ACH(CO ₂ C ₂ H ₅) ₂ (80)
Diethyl methylmalonate	CH ₃ C(A)(CO ₂ C ₂ H ₅) ₂ (70)
Diethyl ethylmalonate	C ₂ H ₅ C(A)(CO ₂ C ₂ H ₅) ₂ (59)
Diethyl n-propylmalonate	n-C ₃ H ₇ C(A)(CO ₂ C ₂ H ₅) ₂ (78)
Diethyl n-butylmalonate	n-C ₄ H ₉ C(A)(CO ₂ C ₂ H ₅) ₂ (80)
Ethyl acetoacetate	CH ₃ COCH(A)CO ₂ C ₂ H ₅ (15)
Ethyl n-propylacetoacetate	CH ₃ COC(A)C(C ₂ H ₅) _n CO ₂ C ₂ H ₅ (16)
Ethyl cyanoacetate	NCCH(A)CO ₂ C ₂ H ₅ (16); NCC(A) ₂ CO ₂ C ₂ H ₅ (18)
Ethyl methylcyanoacetate	NCC(A)(CH ₃)CO ₂ C ₂ H ₅ (89)
Ethyl ethylcyanoacetate	NCC(A)(C ₂ H ₅)CO ₂ C ₂ H ₅ (95)
Ethyl isopropylcyanoacetate	NCC(A)(C ₃ H ₇ -i)CO ₂ C ₂ H ₅ (84)
Ethyl n-butylcyanoacetate	NCC(A)(C ₄ H ₉ -n)CO ₂ C ₂ H ₅ (78)
Benzyl cyanide	C ₆ H ₅ C(A) ₂ CN (8)

Note: References 491–1045 are on pp. 545–555.

† This product is obtained after hydrolysis and decarboxylation

‡ This compound was formed *in situ* from 2-(β-diethylaminoethyl)quinoline methosulfate.§ When this compound was formed *in situ* from 1-(β dimethylaminoethyl)isoquinoline methiodide, a more complex reaction product was obtained

TABLE XXII

DONORS USED IN MICHAEL CONDENSATIONS

Malonates, $RCH(CO_2C_2H_5)_2$: $R = H, Cl, Br, NO_2$, methyl, ethyl, *n*-propyl, *n*-butyl, *n*-hexyl, *n*-octyl, *n*-decyl, *n*-dodecyl, *n*-tetradecyl, *n*-hexadecyl, β -methoxyethyl, β -ethoxyethyl, phenyl, benzyl, phenethyl, 1-naphthyl, 1-naphthylmethyl, β -(1-naphthylethyl), 2-naphthyl, 2-naphthylmethyl, β -(2-naphthylethyl); β -aldehydoethyl, β -aldehydopropyl, acetoxy, formamido, acetamido, phthalimido, $R'O_2CCH_2-$, $(R'O_2C)_2CH-$, $R'O_2CCH(CH_3)-CH(CO_2R')-$, $CH_2=C(CO_2C_2H_5)-$, β -ionylideneacetyl, isobutyryl.

Dibenzyl malonate, malonamide, ethyl malonamate, ethyl malonamidinate, diethyl α -cyano- β -methylsuccinate, diethyl α -cyano- β , β -dimethylglutarate.

Cyanoacetates, $RCH(CN)CO_2C_2H_5$: $R = H$, methyl, ethyl, isopropyl, *n*-butyl, phenyl, phenethyl, β -aldehydoethyl, acetamido, $R'O_2C(CH_2)_3-C(CH_3)(CN)-$.

Acetoacetates, $CH_3COCHRCO_2C_2H_5$: $R = H$, methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isoamyl, hexyl, phenyl, benzyl, allyl; acetoacetanilide. Ethyl iminoacetoacetate, $CH_3C(=NH)CH_2CO_2C_2H_5$, and its *N*-methyl derivative; ethyl iminomethylacetoacetate, $CH_3C(=NH)CH(CH_3)CO_2C_2H_5$.

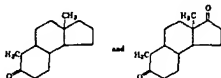
Other ketonic esters: ethyl propionylacetate, butyrylacetate, isobutyrylacetate, hexanoylacetate, γ -ethoxyacetoacetate, palmitoylacetate, stearoylacetate; diethyl acetone-1,3-dicarboxylate, ethyl isobutyrylisobutyrate, ethyl α -acetylsuccinate, ethyl α -acetyladiate, $C_2H_5O_2CCH_2CH_2COCH(CH_3)CO_2C_2H_5$, ethyl benzoylacetate, ethyl 2-oxocyclohexane-1-carboxylate and its 3-methyl derivative, ethyl 2-oxocyclopentane-1-carboxylate and its 5-methyl derivative, higher cycloalkanone-2-carboxylates, 2-carbomethoxy-1-tetralone, methyl 1-keto-1,2,3,4-tetrahydrophenanthrene-2-carboxylate, ethyl camphor-3-carboxylate, 3-ethoxy-5,5-dimethyl-6-carbomethoxy-2-cyclohexen-1-one, ethyl phenylpyruvate (α -keto ester).

Monocarboxylic acid esters: ethyl acetate, ethyl isobutyrate, diethyl glutaconate, diethyl itaconate, ethyl phenylacetate (also *m*- NO_2 , *p*- NO_2 , Cl , Br , and C_2H_5 analogs) and its α -ethyl, *n*-propyl, *n*-butyl, isobutyl derivatives, ethyl furan-2-acetate, ethyl thiophene-2-acetate, ethyl α -naphthylacetate, methyl diphenylacetate, ethyl α -pyridylacetate, triethyl phosphonoacetate, triethyl α -phosphonohexanoate.

Ketones: acetone, methyl ethyl ketone, methyl *n*-propyl ketone,* methyl isopropyl ketone,* methyl isobutyl ketone,* pinacolone, methyl *n*-butyl ketone,* methyl *n*-amyl ketone,* diisopropyl ketone,* diisobutyl ketone, isopropyl *n*-amyl ketone,* isopropyl *n*-nonyl ketone,* methyl β -cyanoethyl ketone, β , β -diethoxyethyl alkyl ketones, acetylacetone, acetonylacetone,* heptadecane-2,4-dione, octadecane-2,4-dione, isobutyrylacetone, diisobutyrylmethane, cyclopentanone, 2-methylcyclopentane-1,3-dione, cyclohexanone,

* Condensed only with acrylonitrile as acceptor.

2-, 3-, and 4-methylcyclohexanone, camphorone, dihydro- and tetrahydrocarvone, carvotanacetone, cyclohexane-1,2-dione, 2-hydroxy- and 2-acetoxycyclohexanone, cyclohexane-1,3-dione and its 2-alkyl derivatives, 5,5-dimethyl-1,3-cyclohexanedione, cyclohexenylcyclohexanone, 2-methyl-6-isopropenylcyclohexanone, 2-aldehydocyclohexanone, 2-aldehydo-4-(*p*-carboxy- and *p*-carbomethoxy-cyclohexyl)cyclohexanone, higher cycloalkanones, 1-tetralone, 2-methyl-1-tetralone, 6-methoxy-1-tetralone, 2-(β -diethylaminoethyl)-1-tetralone, 2-hydroxymethylene-6-methoxy-1-tetralone, *trans*-2-decalone, 1-methyl-2-decalone (*cis* and *trans*) and its 5-methoxy, 6-methoxy, 5,6-dimethoxy, and 6-carbethoxy derivatives, 10-methyl-2-decalone, 9-methyl-8-hydrindanone, anthrone, 4-keto-1,2,3,4-tetrahydropheanthrene, 4-keto-1,2,3,4,9,10,11,12-octahydropheanthrene,* 4,9-diketo-1,2,3,4,9,10,11,12-octahydropheanthrene.*



Acetophenone, phenylacetone, propiophenone, isobutyrophenone, benzoylacetone, dibenzyl ketone, deoxybenzoin, *p*-phenylacetylbiiphenyl, dibenzoylmethane, 1,2-dibenzylethane, α -methyl- α -*n*-butylacetophenone,* α -methyl- α -*n*-octylacetophenone,* α -ethyl- α -*n*-propylacetophenone,* isopropyl benzyl ketone,* α -phenyl- α -*n*-octylacetone,* 2-phenylcyclohexanone and its 6-benzylidene derivative,* 2-aldehydo-4-(*p*-carboxy- and *p*-carbomethoxyphenyl)cyclohexanone, 2-phenylcycloheptanone.

2-Acetylfuran,* 5-methyl-2-acetylfuran,* 2-propionylfuran,* 5-methyl-2-propionylfuran,* 2,5-dimethyl-3-acetylfuran,* 2,5-dimethyl-3-propionylfuran,* 2-butyrylfuran,* 2,5-dimethyl-3-butyrylfuran,* 2-acetyl-, 2-propionyl-, and 2-butyryl-thiophene and their 5-methyl derivatives,* 2-acetoacetylthiophene.*

Acetylacetone imine, benzoylacetone imine, (*p*-methylbenzoyl)acetone imine.

Aldehydes: acetaldehyde,* propionaldehyde,* butyraldehyde, isobutyraldehyde, diethylacetaldehyde,* heptaldehyde, 2-ethylhexanal, diethylacetaldehyde, phenylacetaldehyde, α -phenylpropionaldehyde.*

Nitriles: malononitrile, acetonitrile, propionitrile, cyanacetamide and its *N*-alkyl derivatives, benzyl cyanide and its derivatives nuclearily substituted by *o*-Cl, *m*-Cl, Br, CH₃, NH₂, *p*-Br, CH₃, OCH₃, NO₂; benzyl cyanide α -substituted by methyl, ethyl, isopropyl, *n*-butyl, *n*-pentyl, 3-methylbutyl, (1-cyclohexenyl), cyclohexyl, (*p*-chlorophenyl), (2-thienyl), (2-pyridyl) and β -diethylaminoethyl; diphenylacetone nitrile; diethyl cyanomethanephosphonate, 2-cyanocycloheptanone, CH₂C(=NH)CH₂CN, C₆H₅C(=NH)CH₂CN.

* Condensed only with acrylonitrile as acceptor.

TABLE XXII—*Continued*

DONORS USED IN MICHAEL CONDENSATIONS

Nitro compounds: nitromethane, nitroethane, 1-nitropropane, 2-nitropropane, 1-nitrobutane, 1-nitroisobutane, β,β -dinitroethanol, methyl 2-nitropropyl ether, methyl 2-nitropropyl sulfide, butyl 3-nitrobutyl sulfone, nitrocyclohexane, dinitromethane, phenylnitromethane and its *p*-bromo derivative, methyl 2-nitro-1-phenylpropyl ether, methyl and ethyl nitroacetates, methyl γ,γ -dinitrobutyrate, diethyl nitromalonate, 1,1-dinitroethane.

Sulfones: phenyl benzyl sulfone, *p*-tolyl benzyl sulfone, allyl *p*-tolyl sulfone, ethyl *p*-toluenesulfoacetate, phenacyl *p*-tolyl sulfone, bis(benzene-sulfonyl)methane, bis(methanesulfonyl)methane.

Hydrocarbons and derivatives: cyclopentadiene, divinylmethane, indene, 1-isopropylideneindene, fluorene, 2-nitrofluorene,* 2,7-dibromofluorene, 1-methylfluorene, 9-phenylfluorene, 9-hydroxyfluorene, fluorene-9-carboxylates, ethyl 1-methylfluorene-9-carboxylate, 1,2,3,4-tetrahydrofluoranthene, 2,3,4-trimethyl-1,2-dihydrofluoranthene, 4,5-methylenephenanthrene, methyl 4-cyclopenta[*def*]phenanthrene-4-carboxylate.

Miscellaneous donors (of occasional use): α -aceto- γ -butyrolactone, ethyl oxaloacetate and its α -methyl derivative, ethyl β -methyl- γ -nitrobutyrate, diethyl succinate, isophorone, 1-formyl-2-keto-10-methyl- $\Delta^{3,6}$ -hexahydronaphthalene, α -naphthol (keto form), ethyl 4-hydroxy-2,3-benzofuran-5-carboxylate (keto form), 4-hydroxycoumarin (keto form), 2-hydroxy-1,4-naphthoquinone (keto form), 2-acetyl-5-cyclohexan-1-one, ethyl (3,4-dihydro-1-naphthyl)cyanoacetate, ethyl (1-methyl-1,2,5,6-tetrahydro-4-pyridyl)acetate, α - and γ -picoline, α - and γ -quinaldine, rhodanine, Inhoffen ketone, kojic acid, 1-methyloxindole, 1,3-dimethyloxindole, methyl oxindole-3-propionate, 2,3-dihydro-2-phenylbenzo- γ -pyrone.

* Condensed only with acrylonitrile as acceptor.

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